JC20 Rec'd PCT/PTO 24 AUG 2001

FORM PTO-1390 (REV 11-2000)	U S DEPARTMENT OF COM[illegible] PATENT AND TRADEMARK OFFICE	ATTORN[illegible]OCKET NUMBER 468-30

TRANSMITTAL LETTER TO THE UNITED STATES DESIGNATED/ELECTED OFFICE (DO/EO/US) CONCERNING A FILING UNDER 35 U.S.C. 371

U.S APPLICATION NO (If known, see 37 C.F.R. 1.5): 09/914286 Unknown

INTERNATIONAL APPLICATION NO.	INTERNATIONAL FILING DATE	PRIORITY DATE CLAIMED
PCT/JP00/01041	23 February 2000	24 February 1999

TITLE OF INVENTION

AVERMECTIN AGLYCON SYNTHASE GENES

APPLICANT(S) FOR DO/EO/US

OMURA et al.

Applicant herewith submits to the United States Designated/Elected Office (DO/EO/US) the following items and other information:

1. ☒ This is a **FIRST** submission of items concerning a filing under 35 U.S.C. 371.
2. ☐ This is a **SECOND** or **SUBSEQUENT** submission of items concerning a filing under 35 U.S.C. 371.
3. ☒ This is an express request to begin national examination procedures (35 U.S.C. 371(f)). The submission must include items (5), (6), (9) and (21) indicated below.
4. ☒ The U.S. has been elected by the expiration of 19 months from the priority date (Article 31).
5. A copy of the International Application as filed (35 U.S.C. 371(c)(2)).
 - a. ☐ is attached hereto (required only if not communicated by the International Bureau).
 - b. ☒ has been communicated by the International Bureau.
 - c. ☐ is not required, as the application was filed in the United States Receiving Office (RO/US).
6. ☒ An English language translation of the International Application as filed (35 U.S.C. 371(c)(2)).
 - a. ☒ is attached hereto.
 - b. ☐ has been previously submitted under 35 U.S.C. 154(d)(4).
7. ☐ Amendments to the claims of the International Application under PCT Article 19 (35 U.S.C. 371(c)(3))
 - a. ☐ are attached hereto (required only if not communicated by the International Bureau).
 - b. ☐ have been communicated by the International Bureau.
 - c. ☐ have not been made; however, the time limit for making such amendments has **NOT** expired.
 - d. ☐ have not been made and will not be made.
8. ☐ An English language translation of the amendments to the claims under PCT Article 19 (35 U.S.C. 371(c)(3)).
9. ☒ An oath or declaration of the inventor(s) (35 U.S.C. 371(c)(4)).
10. ☐ A English language translation of the annexes of the International Preliminary Examination Report under PCT Article 36 (35 U.S.C. 371(c)(5)).

Items 11 To 20 below concern document(s) or information included:

11. ☒ An Information Disclosure Statement under 37 C.F.R. 1.97 and 1.98.
12. ☒ An assignment document for recording. A separate cover sheet in compliance with 37 C.F.R. 3.28 and 3.31 is included.
13. ☐ A FIRST preliminary amendment.
14. ☐ A SECOND or SUBSEQUENT preliminary amendment.
15. ☐ A substitute specification.
16. ☐ A change of power of attorney and/or address letter.
17. ☐ A computer-readable form of the sequence listing in accordance with PCT Rule 13ter.2 and 35 U.S.C. 1.821-1.825.
18. ☐ A second copy of the published international application under 35 U.S.C. 154(d)(4).
19. ☐ A second copy of the English language translation of the international application under 35 U.S.C. 154(d)(4).
20. ☒ Other items or information. Sequence Listing (245 pages) / Front page of the PCT Publication

554102

518 Rec'd PCT/PTO 24 AUG 2001

U.S. APPLICATION NO. (If known, see 37 C.F.R. 1.5)	INTERNATIONAL APPLICATION NO.	ATTORNEY'S DOCKET NUMBER
09/914286 Unknown	PCT/JP00/01041	468-30

21. ☒ The following fees are submitted:

	CALCULATIONS PTO USE ONLY		
BASIC NATIONAL FEE (37 C.F.R. 1.492(a)(1)-(5):			
-- Neither international preliminary examination fee (37 C.F.R. 1.482) nor international search fee (37 C.F.R. 1.445(a)(2)) paid to USPTO and International Search Report not prepared by the EPO or JPO $1000.00			
-- International preliminary examination fee (37 C.F.R. 1.482) not paid to USPTO but International Search Report prepared by the EPO or JPO $860.00			
-- International preliminary examination fee (37 C.F.R. 1.482) not paid to USPTO but international search fee (37 C.F.R. 1.445(a)(2)) paid to USPTO $710.00			
-- International preliminary examination fee (37 C.F.R. 1.482) paid to USPTO but all claims did not satisfy provisions of PCT Article 33(1)-(4) $690.00			
-- International preliminary examination fee (37 C.F.R. 1.482) paid to USPTO and all claims satisfied provisions of PCT Article 33(1)-(4) $100.00			
ENTER APPROPRIATE BASIC FEE AMOUNT =	$	860.00	
Surcharge of $130.00 for furnishing the oath or declaration later than ☐ 20 ☐ 30 months from the earliest claimed priority date (37 C.F.R. 1.492(e)).	$	0.00	

CLAIMS	NUMBER FILED		NUMBER EXTRA	RATE			
Total Claims	57	-20 =	37	X	$18.00	$	666.00
Independent Claims	17	-3 =	14	X	$80.00		1120.00
MULTIPLE DEPENDENT CLAIMS(S) (if applicable)					$270.00	$	270.00
					TOTAL OF ABOVE CALCULATIONS =	$	**2916.00**
☐ Applicant claims small entity status. See 37 CFR 1.27. The fees indicated above are reduced by 1/2.							0.00
					SUBTOTAL =	$	**2916.00**
Processing fee of $130.00, for furnishing the English Translation later than ☐ 20 ☐ 30 months from the earliest claimed priority date (37 C.F.R. 1.492(f)). +							0.00
					TOTAL NATIONAL FEE =	$	**2916.00**
Fee for recording the enclosed assignment (37 C.F.R. 1.21(h)). The assignment must be accompanied by an appropriate cover sheet (37 C.F.R. 3.28, 3.31). **$40.00** per property +						$	40.00
Fee for Petition to Revive Unintentionally Abandoned Application ($1240.00 – Small Entity = $620.00)						$	0.00
					TOTAL FEES ENCLOSED =	$	**2956.00**
					Amount to be: refunded	$	
					Charged	$	

a. ☒ A check in the amount of $2956.00 to cover the above fees is enclosed.
b. ☐ Please charge my Deposit Account No. 14-1140 in the amount of $_____ to cover the above fees. A duplicate copy of this form is enclosed.
c. ☒ The Commissioner is hereby authorized to charge any additional fees which may be required, or credit any overpayment to Deposit Account No. 14-1140. A duplicate copy of this form is enclosed.
d. ☒ The entire content of the foreign application(s), referred to in this application is/are hereby incorporated by reference in this application.

NOTE: Where an appropriate time limit under 37 C.F.R. 1.494 or 1.495 has not been met, a petition to revive (37 C.F.R. 1.137(a) or (b)) must be filed and granted to restore the application to pending status.

SEND ALL CORRESPONDENCE TO:

NIXON & VANDERHYE P.C.
1100 North Glebe Road, 8th Floor
Arlington, Virginia 22201-4714
Telephone: (703) 816-4000

SIGNATURE

Arthur R. Crawford
NAME

25,327 REGISTRATION NUMBER

August 24, 2001 Date

554102

OIPE JC98 DEC 07 2001 PATENT & TRADEMARK OFFICE

Rec'd PCT/PTO 07 DEC 2001

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re Patent Application of

OMURA et al.

Appln. No. 09/914,286

Filed: August 24, 2001

FOR: AVERMECTIN AGLYCON SYNTHASE GENES

Atty. Ref.: 468-30

Group Art Unit: Not Known

Examiner: Not Known

* * *

PRELIMINARY AMENDMENT AND SUBMISSION OF SEQUENCE LISTING

December 7, 2001

Hon. Commissioner for Patents
Washington, D.C. 20231

Sir:

In response to the Notification of Missing Requirements mailed October 9, 2001, entry of the following amendments and remarks is respectfully requested.

IN THE SPECIFICATION

Kindly enter the following new paragraph.

Page 1, insert as the first paragraph following the title,

This is a national stage application under 35 U.S.C. 371 of PCT/JP00/01041, filed on February 23, 2000, now abandoned.

The specification is amended as follows.

Page 8, first paragraph starting on line 1,

(12) The DNA according to the above (4) wherein the DNA encoding a polypeptide having β-ketoacyl-ACP synthase activity is:

a DNA comprising the nucleotide sequence selected from the group consisting of nucleotide Nos. 1441-2742, 6256-7545, 12076-13368, 15217-16506, 20008-21297 and 24781-26079 of SEQ ID NO: 1, and nucleotide Nos. 100-1383, 4771-6060, 7906-9258, 14935-16224, 20413-21705 and 25810-27102 of SEQ ID NO: 2; or

a DNA which hybridizes with this DNA under stringent conditions and which encodes a polypeptide having β-ketoacyl-ACP synthase activity.

Page 11, fifth paragraph starting on line 29 and continuing to page 12,

(26) A DNA comprising the nucleotide sequence selected from the group consisting of nucleotide Nos. 1441-2742, 6256-7545, 12076-13368, 15217-16506, 20008-21297 and 24781-26079 of SEQ ID NO: 1, and nucleotide Nos. 100-1383, 4771-6060, 7906-9258, 14935-16224, 20413-21705, and 25810-27102 of SEQ ID NO: 2; or

a DNA which hybridizes with this DNA under stringent conditions and which encodes a polypeptide having β-ketoacyl-ACP synthase activity.

Page 13, fourth paragraph starting on line 21 and continuing to page 14,

(33) A polypeptide comprising the amino acid sequence selected from the group consisting of amino acid Nos. 29-344, 366-451, 481-914, 1050-1356, 1715-1892, 1979-2060, 2086-2515, 2983-3128, 3537-3714 and 3805-3886 of SEQ ID NO: 3, amino acid Nos. 36-466, 596-908, 978-1059, 1083-1512, 1653-1964, 2306-2483, 2575-2656, 2680-3109, 3230-3538, 3878-4056, 4159-4240, 4271-4703, 4815-5122, 5168-5307, 5753-5930 and 6032-6113 of SEQ ID NO: 4, amino acid Nos. 34-461, 550-891, 1212-1396, 1483-1564, 1591-2020, 2108-2448, 2525-2606, 2636-3086, 3226-3591, 3629-3763, 4183-4363, 4460-4553 and 4627-4873 of SEQ ID NO: 5, amino acid Nos. 38-467, 574-914, 956-1081, 1488-1673, 1756-1837, 1864-2294, 2390-2732, 2776-2902, 3288-3473, 3556-3637, 3663-4093, 4182-4523, 4565-4685, 5085-5270 and 5353-5434 of SEQ ID NO: 6; or

a polypeptide comprising an amino acid sequence wherein one or more amino acids are deleted, replaced or added in the amino acid sequence selected above, and having avermectin aglycon synthase domain activity.

Page 24, fourth paragraph starting on line 25 and continuing to page 25,

in SEQ ID NO: 4,
KS3: 36 to 466,
AT3: 596 to 908,
ACP3: 978 to 1059,
KS4: 1083 to 1512,
AT4: 1653 to 1964,
KR4: 2306 to 2483,
ACP4: 2575 to 2656,
KS5: 2680 to 3109,
AT5: 3230 to 3538,
KR5: 3878 to 4056,
ACP5: 4159 to 4240,
KS6: 4271 to 4703,
AT6: 4815 to 5122,
DH6: 5168 to 5307
KR6: 5753 to 5930,
ACP6: 6032 to 6113;

Page 26, third paragraph starting on line 21,

In other words, based on the above module, domain and ORF information obtained from DNAs having nucleotide sequences of SEQ ID NO: 1 and 2 derived from *Streptomyces avermitilis*, modules, domains and ORFs, which are relevant to the Avermectin aglycon synthase genes derived from other bacteria capable of producing avermectin, can be determined.

Page 35, first paragraph starting on line 1,

Specific examples include SP2/O, NSO and the like for mouse myeloma cells, YB2/O and the like for rat myeloma cells, HEK293 (ATCC: CRL-1573) and the like for

human fetal kidney cells, BALL-1 and the like for human leukemia cells, and COS-1, COS-7 and the like for African green monkey kidney cells.

Page 43, fifth paragraph starting on line 22,

Examples of the thus obtained protein include a protein comprising the amino acid sequences represented by SEQ ID NOS:3, 4, 5 and 6.

Page 43, sixth paragraph starting on line 25 and continuing to page 44,

Furthermore, a fusion protein of the protein of the present invention and other protein may be produced, and purified by affinity chromatography using a substance having affinity to the fusion protein. For example, the protein of the present invention may be produced as a fusion protein with protein A according to the method of Lowe *et al.* (*Proc. Natl. Acad. Sci. USA, 86*: 8227 (1989); *Genes Develop., 4*: 1288 (1990)), or the method described in Japanese Published Unexamined Patent Application No. 336963/93 or WO 94/23021, and purified by affinity chromatography using immunoglobulin G.

IN THE CLAIMS

Kindly enter the following amended claims.

12. (Amended) The DNA according to claim 4 wherein the DNA encoding a polypeptide having β-ketoacyl-ACP synthase activity is:
a DNA comprising comprising the nucleotide sequence selected from the group consisting of nucleotide Nos. 1441-2742, 6256-7545, 12076-13368, 15217-16506, 20008-21297 and 24781-26079 of SEQ ID NO: 1, and nucleotide Nos. 100-1383, 4771-6060, 7906-9258, 14935-16224, 20413-21705 and 25810-27102 of SEQ ID NO: 2; or
a DNA which hybridizes with said DNA under stringent conditions and which encodes a polypeptide having β-ketoacyl-ACP synthase activity.

26. (Amended) A DNA comprising the nucleotide sequence selected from the group consisting of nucleotide Nos. 1441-2742, 6256-7545, 12076-13368, 15217-16506, 20008-21297, and 24781-26079 of SEQ ID NO: 1 and nucleotide Nos. 100-1383, 4771-6060, 7906-9258, 14935-16224, 20413-21705 and 25810-27102 of SEQ ID NO: 2; or

a DNA which hybridizes with said DNA under stringent conditions and which encodes a polypeptide having β-ketoacyl-ACP synthase activity

33. (Amended) A polypeptide comprising the amino acid sequence selected from the group consisting of amino acid Nos. 29-344, 366-451, 481-914, 1050-1356, 1715-1892, 1979-2060, 2086-2515, 2983-3128, 3537-3714 and 3805-3886 of SEQ ID NO: 3, amino acid Nos. 36-466, 596-908, 978-1059, 1083-1512, 1653-1964, 2306-2483, 2575-2656, 2680-3109, 3230-3538, 3878-4056, 4159-4240, 4271-4703, 4815-5122, 5168-5307, 5753-5930 and 6032-6113 of SEQ ID NO: 4, amino acid Nos. 34-461, 550-891, 1212-1396, 1483-1564, 1591-2020, 2108-2448, 2525-2606, 2636-3086, 3226-3591, 3629-3763, 4183-4363, 4460-4553 and 4627-4873 of SEQ ID NO: 5, amino acid Nos. 38-467, 574-914, 956-1081, 1488-1673, 1756-1837, 1864-2294, 2390-2732, 2776-2902, 3288-3473, 3556-3637, 3663-4093, 4182-4523, 4565-4685, 5085-5270 and 5353-5434 of SEQ ID NO: 6; or

a polypeptide comprising an amino acid sequence wherein one or more amino acida are deleted, replaced or added in the amino acid sequence selected above, and having avermectin aglycon synthase domain activity.

IN THE SEQUENCE LISTING

Kindly enter the attached substitute paper and computer readable forms of the Sequence Listing in lieu of the Sequence Listing submitted on August 24, 2001.

REMARKS

Claims 1-43 are pending.

Substitute paper and original computer readable forms of the Sequence Listing are being submitted herewith in response to the requirement under 35 U.S.C. 371 to comply with the Sequence Rules 37 CFR § 1.821 et seq. The attached substitute paper and original computer readable forms of the Sequence Listing do not add new matter, and their contents are the same. Typographical errors in the length of SEQ ID NOS:1 and 7 have been corrected. Prompt notice of any defects in the Sequence Listing is earnestly solicited and additional time is requested to comply.

A statement claiming priority under 35 U.S.C. 371 is added after the title. Furthermore, errors in the specification are being corrected.

Applicants earnestly solicit an early examination on the merits. The Examiner is invited to contact the undersigned if any further information is required.

Respectfully submitted,

NIXON & VANDERHYE P.C.

By: _____

Gary R. Tanigawa
Reg. No. 43,180

1100 North Glebe Road, 8th Floor
Arlington, VA 22201-4714
Telephone: (703) 816-4000
Facsimile: (703) 816-4100

APPENDIX

MARKED-UP VERSION TO SHOW CHANGES

IN THE SPECIFICATION

The following new paragraph is added on page 1 after the title:

This is a national stage application under 35 U.S.C. 371 of PCT/JP00/01041, filed on February 23, 2000, now abandoned.

The specification is amended as follows.

Page 8, first paragraph starting on line 1,

(12) The DNA according to the above (4) wherein the DNA encoding a polypeptide having β-ketoacyl-ACP synthase activity is:
a DNA comprising the nucleotide sequence selected from the group consisting of nucleotide Nos. 1441-2742, 6256-7545, 12076-13368, 15217-16506, 20008-21297 and 24781-26079 of SEQ ID NO: 1, and nucleotide Nos. 100-1383, 4771-6060, 7906-9258, 14935-16224, 20413-21705 and 25810-27102 of [SEQ ID NO:1] SEQ ID NO: 2; or
a DNA which hybridizes with this DNA under stringent conditions and which encodes a polypeptide having β-ketoacyl-ACP synthase activity.

Page 11, fifth paragraph starting on line 29 and continuing to page 12,

(26) A DNA comprising the nucleotide sequence selected from the group consisting of nucleotide Nos. 1441-2742, 6256-7545, 12076-13368, 15217-16506, 20008-21297 and 24781-26079 of SEQ ID NO: 1, and nucleotide Nos. 100-1383, 4771-6060, 7906-9258, 14935-16224, 20413-21705, and 25810-27102 of [SEQ ID NO: 1] SEQ ID NO: 2; or
a DNA which hybridizes with this DNA under stringent conditions and which encodes a polypeptide having β-ketoacyl-ACP synthase activity.

Page 13, fourth paragraph starting on line 21 and continuing to page 14,

(33) A polypeptide comprising the amino acid sequence selected from the group consisting of amino acid Nos. 29-344, 366-451, 481-914, 1050-1356, 1715-1892, 1979-2060, 2086-2515, 2983-3128, 3537-3714 and 3805-3886 of SEQ ID NO: 3, amino acid Nos. 36-466, 596-908, 978-1059, 1083-1512, 1653-1964, 2306-2483, 2575-2656, 2680-3109, [32030-3538] 3230-3538, 3878-4056, 4159-4240, 4271-4703, 4815-5122, 5168-5307, 5753-5930 and 6032-6113 of SEQ ID NO: 4, amino acid Nos. 34-461, 550-891, 1212-1396, 1483-1564, 1591-2020, 2108-2448, 2525-2606, 2636-3086, 3226-3591, 3629-3763, 4183-4363, 4460-4553 and 4627-4873 of SEQ ID NO: 5, amino acid Nos. 38-467, 574-914, 956-1081, 1488-1673, 1756-1837, 1864-2294, 2390-2732, 2776-2902, 3288-3473, 3556-3637, 3663-4093, 4182-4523, 4565-4685, 5085-5270 and 5353-5434 of SEQ ID NO: 6; or
a polypeptide comprising an amino acid sequence wherein one or more amino acids are deleted, replaced or added in the amino acid sequence selected above, and having avermectin aglycon synthase domain activity.

Page 24, fourth paragraph starting on line 25 and continuing to page 25,
in SEQ ID NO: 4,
KS3: 36 to 466,
AT3: 596 to 908,
ACP3: 978 to 1059,
KS4: 1083 to 1512,
AT4: 1653 to 1964,
KR4: 2306 to 2483,
ACP4: 2575 to 2656,
KS5: 2680 to 3109,
AT5: [32030 to 3538] 3230 to 3538,
KR5: 3878 to 4056,
ACP5: 4159 to 4240,
KS6: 4271 to 4703,
AT6: 4815 to 5122,

DH6: 5168 to 5307

[DH6: 5753 to 5930] KR6: 5753 to 5930,

ACP6: 6032 to 6113;

Page 26, third paragraph starting on line 21,

In other words, based on the above module, domain and ORF information obtained from DNAs having nucleotide sequences of SEQ ID NO: 1 and 2 derived from *Streptomyces avermitilis*, modules, domains and ORFs, which are relevant to the Avermectin aglycon synthase genes [of the present invention] derived from other bacteria capable of producing avermectin, can be determined.

Page 35, first paragraph starting on line 1,

Specific examples include SP2/O, NSO and the like for mouse myeloma cells, YB2/O and the like for rat myeloma cells, HEK293 (ATCC: CRL-1573)[, 293] and the like for human fetal kidney cells, BALL-1 and the like for human leukemia cells, and COS-1, COS-7 and the like for African green monkey kidney cells.

Page 43, fifth paragraph starting on line 22,

Examples of the thus obtained protein include a protein comprising [the amino acid sequence represented by SEQ ID NO:1] the amino acid sequences represented by SEQ ID NOS:3, 4, 5 and 6.

Page 43, sixth paragraph starting on line 25 and continuing to page 44,

Furthermore, a fusion protein of the protein of the present invention and other protein may be produced, and purified by affinity chromatography using a substance having affinity to the fusion protein. For example, the protein of the present invention may be produced as a fusion protein with protein A according to the method of Lowe *et al.* (*Proc. Natl. Acad. Sci. USA*, *86*: 8227 (1989); *Genes Develop.*, *4*: 1288 (1990)), or the method described in Japanese Published Unexamined Patent Application No.

336963/93 or [823021/94] WO 94/23021, and purified by affinity chromatography using immunoglobulin G.

IN THE CLAIMS

The claims are amended as follows.

12. (Amended) The DNA according to claim 4 wherein the DNA encoding a polypeptide having β-ketoacyl-ACP synthase activity is:
a DNA comprising comprising the nucleotide sequence selected from the group consisting of nucleotide Nos. 1441-2742, 6256-7545, 12076-13368, 15217-16506, 20008-21297 and 24781-26079 of SEQ ID NO: 1, and nucleotide Nos. 100-1383, 4771-6060, 7906-9258, 14935-16224, 20413-21705 and 25810-27102 of [SEQ ID NO: 1] SEQ ID NO: 2; or
a DNA which hybridizes with said DNA under stringent conditions and which encodes a polypeptide having β-ketoacyl-ACP synthase activity.

26. (Amended) A DNA comprising the nucleotide sequence selected from the group consisting of nucleotide Nos. 1441-2742, 6256-7545, 12076-13368, 15217-16506, 20008-21297, and 24781-26079 of SEQ ID NO: 1 and nucleotide Nos. 100-1383, 4771-6060, 7906-9258, 14935-16224, 20413-21705 and 25810-27102 of [SEQ ID NO: 1] SEQ ID NO: 2; or
a DNA which hybridizes with said DNA under stringent conditions and which encodes a polypeptide having β-ketoacyl-ACP synthase activity

33. (Amended) A polypeptide comprising the amino acid sequence selected from the group consisting of amino acid Nos. 29-344, 366-451, 481-914, 1050-1356, 1715-1892, 1979-2060, 2086-2515, 2983-3128, 3537-3714 and 3805-3886 of SEQ ID NO: 3, amino acid Nos. 36-466, 596-908, 978-1059, 1083-1512, 1653-1964, 2306-2483, 2575-2656, 2680-3109, [32030-3538] 3230-3538, 3878-4056, 4159-4240, 4271-4703, 4815-5122, 5168-5307, 5753-5930 and 6032-6113 of SEQ ID NO: 4, amino acid

Nos. 34-461, 550-891, 1212-1396, 1483-1564, 1591-2020, 2108-2448, 2525-2606, 2636-3086, 3226-3591, 3629-3763, 4183-4363, 4460-4553 and 4627-4873 of SEQ ID NO: 5, amino acid Nos. 38-467, 574-914, 956-1081, 1488-1673, 1756-1837, 1864-2294, 2390-2732, 2776-2902, 3288-3473, 3556-3637, 3663-4093, 4182-4523, 4565-4685, 5085-5270 and 5353-5434 of SEQ ID NO: 6; or

a polypeptide comprising an amino acid sequence wherein one or more amino acida are deleted, replaced or added in the amino acid sequence selected above, and having avermectin aglycon synthase domain activity.

IN THE SEQUENCE LISTING

The substitute paper and original computer readable forms of the Sequence Listing are attached.

09914286 - 090101

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

PCT

In re Patent Application of

OMURA et al.

Atty Dkt. 462-30 C# M#

Group Art Unit: Not Known

Appln. No. 09/914,286

Examiner: Not Known

Filed: August 24, 2001

Date: December 7, 2001

Title: AVERMECTIN AGLYCONE SYNTHASE GENES

OIPE DEC 07 2001 PATENT & TRADEMARK OFFICE

Rec'd PCT/PTO 07 DEC 2001

Assistant Commissioner for Patents
Washington, DC 20231

Sir:

PRELIMINARY AMENDMENT AND SUBMISSION OF SEQUENCE LISTING

This is a response/amendment/letter in the above-identified application and includes an attachment which is hereby incorporated by reference and the signature below serves as the signature to the attachment in the absence of any other signature thereon.

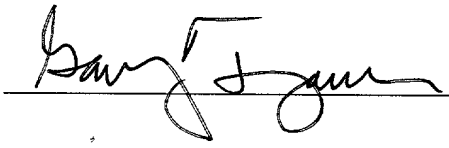
Fees are attached as calculated below:

Total effective claims after amendment **57** minus highest number previously paid for **57** (at least 20) = 0 x $	$	0.00
Independent claims after amendment **17** minus highest number previously paid for **17** (at least 3) = 0 x $	$	0.00
If proper multiple dependent claims now added for first time, add $ (ignore improper)	$	0.00
Petition is hereby made to extend the current due date so as to cover the filing date of this paper and attachment(s) ($ /1 month; $ /2 months; $ /3 months)	$	0.00
Terminal disclaimer enclosed, add $	$	0.00
☐ First/second submission after Final Rejection pursuant to 37 CFR 1.129(a) ($) ☐ Please enter the previously unentered , filed ☐ Submission attached	$	0.00
Subtotal	$	**0.00**
If "small entity," then enter half (1/2) of subtotal and subtract ☐ Applicant claims "small entity" status. ☐ Statement filed herewith	-$	0.00
Rule 56 Information Disclosure Statement Filing Fee ($)	$	0.00
Assignment Recording Fee ($)	$	0.00
Other: **PAPER COPY OF SEQUENCE LISTING AND FLOPPY DISK IN COMPUTER READABLE FORM**		**0.00**
TOTAL FEE ENCLOSED	$	**0.00**

The Commissioner is hereby authorized to charge any deficiency, or credit any overpayment, in the fee(s) filed, or asserted to be filed, or which should have been filed herewith (or with any paper hereafter filed in this application by this firm) to our Account No. 14-1140. A duplicate copy of this sheet is attached.

1100 North Glebe Road, 8th Floor
Arlington, Virginia 22201-4714
Telephone: (703) 816-4000
Facsimile: (703) 816-4100
GRT:ap

NIXON & VANDERHYE P.C.
By Atty: Gary R. Tanigawa, Reg. No. 43,180

Signature: 

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

OIPE
DEC 07 2001
PATENT & TRADEMARK OFFICE

In re Patent Application of: OMURA et al.
Appln. No. 09/914,286
Filed: August 24, 2001
Title: AVERMECTIN AGLYCON SYNTHASE GENES

Atty Dkt. 468-30
C# M#
Group Art Unit: Not Known
Examiner: Not Known
Date: December 7, 2001

Assistant Commissioner for Patents
Washington, DC 20231

Sir:

PRELIMINARY AMENDMENT AND SUBMISSION OF SEQUENCE LISTING

This is a response/amendment/letter in the above-identified application and includes an attachment which is hereby incorporated by reference and the signature below serves as the signature to the attachment in the absence of any other signature thereon.

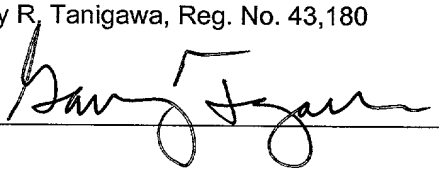
Fees are attached as calculated below:

Total effective claims after amendment **57** minus highest number previously paid for **57** (at least 20) = 0 x $	$	0.00
Independent claims after amendment **17** minus highest number previously paid for **17** (at least 3) = 0 x $	$	0.00
If proper multiple dependent claims now added for first time, add $ (ignore improper)	$	0.00
Petition is hereby made to extend the current due date so as to cover the filing date of this paper and attachment(s) ($ /1 month; $ /2 months; $ /3 months)	$	0.00
Terminal disclaimer enclosed, add $	$	0.00
☐ First/second submission after Final Rejection pursuant to 37 CFR 1.129(a) ($) ☐ Please enter the previously unentered , filed ☐ Submission attached	$	0.00
Subtotal	$	**0.00**
If "small entity," then enter half (1/2) of subtotal and subtract ☐ Applicant claims "small entity" status. ☐ Statement filed herewith	-$	0.00
Rule 56 Information Disclosure Statement Filing Fee ($)	$	0.00
Assignment Recording Fee ($)	$	0.00
Other: **PAPER COPY OF SEQUENCE LISTING AND FLOPPY DISK IN COMPUTER READABLE FORM**		**0.00**
TOTAL FEE ENCLOSED	$	**0.00**

The Commissioner is hereby authorized to charge any deficiency, or credit any overpayment, in the fee(s) filed, or asserted to be filed, or which should have been filed herewith (or with any paper hereafter filed in this application by this firm) to our Account No. 14-1140. A duplicate copy of this sheet is attached.

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NIXON & VANDERHYE P.C.
By Atty: Gary R. Tanigawa, Reg. No. 43,180

Signature: 

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DEC 0 7 2001
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SEQUENCE LISTING

<110> OMURA, Satoshi
IKEDA, Haruo

<120> AVERMECTIN AGLYCON SYNTHASE GENES

<130> 468-30/PH-775-PCT

<140> US 09/914,286
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Val Leu Gly Val Ala Asp Glu Ala Asp Gly Gly Val Val Phe Val Phe
             20                  25                  30

ccc ggg cag ggc ccg caa tgg ccg ggc atg gga agg gaa ctt ctc gac   144
Pro Gly Gln Gly Pro Gln Trp Pro Gly Met Gly Arg Glu Leu Leu Asp
         35                  40                  45

gct tcc gac gtc ttc cgg gag agc gtc cgc gcc tgc gaa gcc gcg ttc   192
Ala Ser Asp Val Phe Arg Glu Ser Val Arg Ala Cys Glu Ala Ala Phe
     50                  55                  60

gcg ccc tac gtc gac tgg tcg gtg gag cag gtg ttg cgg gac tcg ccg   240
Ala Pro Tyr Val Asp Trp Ser Val Glu Gln Val Leu Arg Asp Ser Pro
 65                  70                  75                  80

gac gct ccc ggg ctg gac cgg gtg gac gtc gtc cag ccg acc ctg ttc   288
Asp Ala Pro Gly Leu Asp Arg Val Asp Val Val Gln Pro Thr Leu Phe
                 85                  90                  95
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gcc gtc atg atc tcc ctg gcc gcc ctc tgg cgc tcg caa ggg gtc gag   336
Ala Val Met Ile Ser Leu Ala Ala Leu Trp Arg Ser Gln Gly Val Glu
            100                 105                 110

ccg tgc gcg gtg ctg gga cac agc ctg ggc gag atc gcg gca gcc cac   384
Pro Cys Ala Val Leu Gly His Ser Leu Gly Glu Ile Ala Ala Ala His
        115                 120                 125

gtc tcg gga ggc ctg tcc ctg gcc gac gcc gca cgc gtg gtg acg ctt   432
Val Ser Gly Gly Leu Ser Leu Ala Asp Ala Ala Arg Val Val Thr Leu
    130                 135                 140

tgg agc cag gca cag acc acc ctt gcc ggg acc ggc gcg ctc gtc tcc   480
Trp Ser Gln Ala Gln Thr Thr Leu Ala Gly Thr Gly Ala Leu Val Ser
145                 150                 155                 160

gtc gcc gcc acg ccg gat gag ctc ctg ccc cga atc gct ccg tgg acc   528
Val Ala Ala Thr Pro Asp Glu Leu Leu Pro Arg Ile Ala Pro Trp Thr
                165                 170                 175

gag gac aac ccg gcg cgg ctc gcc gtc gca gcc gtc aac gga ccc cgg   576
Glu Asp Asn Pro Ala Arg Leu Ala Val Ala Ala Val Asn Gly Pro Arg
            180                 185                 190

agc aca gtc gtt tcc ggt gcc cgc gag gcc gtc gcg gac ctg gtg gcc   624
Ser Thr Val Val Ser Gly Ala Arg Glu Ala Val Ala Asp Leu Val Ala
        195                 200                 205

gac ctc acc gcc gcg cag gtg cgc acg cgc atg atc ccg gtg gac gtt   672
Asp Leu Thr Ala Ala Gln Val Arg Thr Arg Met Ile Pro Val Asp Val
    210                 215                 220

ccc gcc cac tcc ccc ctg atg tac gcc atc gag gaa cgg gtc gtc agc   720
Pro Ala His Ser Pro Leu Met Tyr Ala Ile Glu Glu Arg Val Val Ser
225                 230                 235                 240

ggc ctg ctg ccc atc acc cca cgc ccc tcc cgc atc ccc ttc cac tcc   768
Gly Leu Leu Pro Ile Thr Pro Arg Pro Ser Arg Ile Pro Phe His Ser
                245                 250                 255

tcg gtg acc ggc ggc cgc ctc gac acc cgc gag cta gac gcg gcg tac   816
Ser Val Thr Gly Gly Arg Leu Asp Thr Arg Glu Leu Asp Ala Ala Tyr
            260                 265                 270

tgg tac cgc aac atg tcg agc acg gtc cgg ttc gag ccc gcc gcc cgg   864
Trp Tyr Arg Asn Met Ser Ser Thr Val Arg Phe Glu Pro Ala Ala Arg
        275                 280                 285

ctg ctt ctg cag cag ggg ccc aag acg ttc gtc gag atg agc ccg cac   912
Leu Leu Leu Gln Gln Gly Pro Lys Thr Phe Val Glu Met Ser Pro His
    290                 295                 300

ccg gtg ctg acc atg ggc ctc cag gag ctc gcc ccg gac ctg ggc gac   960
Pro Val Leu Thr Met Gly Leu Gln Glu Leu Ala Pro Asp Leu Gly Asp
305                 310                 315                 320

acc acc ggc acc gcc gac acc gtg atc atg ggc acg ctg cgc cgc ggc  1008
Thr Thr Gly Thr Ala Asp Thr Val Ile Met Gly Thr Leu Arg Arg Gly
                325                 330                 335
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cag ggc acc ctg gac cac ttc ctg acg tct ctc gcc caa cta cgg ggg   1056
Gln Gly Thr Leu Asp His Phe Leu Thr Ser Leu Ala Gln Leu Arg Gly
            340                 345                 350

cat ggt gag acg tcg gcg acc acc gtc ctc tcg gca cgc ctg acc gcg   1104
His Gly Glu Thr Ser Ala Thr Thr Val Leu Ser Ala Arg Leu Thr Ala
        355                 360                 365

ctg tcc ccc acg cag cag cag tcg ctg ctc ctg gac ctg gtg cgc gcc   1152
Leu Ser Pro Thr Gln Gln Gln Ser Leu Leu Leu Asp Leu Val Arg Ala
    370                 375                 380

cac acc atg gcg gtg ctg aac gac gac gga aac gag cgc acc gcg tcg   1200
His Thr Met Ala Val Leu Asn Asp Asp Gly Asn Glu Arg Thr Ala Ser
385                 390                 395                 400

gat gcc ggc cca tcg gcg agt ttc gcc cac ctc ggc ttc gac tcc gtc   1248
Asp Ala Gly Pro Ser Ala Ser Phe Ala His Leu Gly Phe Asp Ser Val
                405                 410                 415

atg ggt gtc gaa ctg cgc aac cgc ctc agc aag gcc acg ggc ctg cgg   1296
Met Gly Val Glu Leu Arg Asn Arg Leu Ser Lys Ala Thr Gly Leu Arg
            420                 425                 430

ttg ccc gtg acg ctc atc ttc gac cac acc acg ccg gcc gcg gtc gcc   1344
Leu Pro Val Thr Leu Ile Phe Asp His Thr Thr Pro Ala Ala Val Ala
        435                 440                 445

gcg cgc ctt cgg acc gcg gcg ctc ggc cac ctc gac gag gac acc gcg   1392
Ala Arg Leu Arg Thr Ala Ala Leu Gly His Leu Asp Glu Asp Thr Ala
    450                 455                 460

ccc gta ccg gac tca ccc agc ggc cac gga ggc acg gca gcg gcg gac   1440
Pro Val Pro Asp Ser Pro Ser Gly His Gly Gly Thr Ala Ala Ala Asp
465                 470                 475                 480

gac ccg atc gcc atc atc ggc atg gca tgc cgt ttc ccg ggc gga gtc   1488
Asp Pro Ile Ala Ile Ile Gly Met Ala Cys Arg Phe Pro Gly Gly Val
                485                 490                 495

cgg tcc ccg aag gac ctg tgg gag ctg gcc gcc tcg ggc gga gac gcc   1536
Arg Ser Pro Lys Asp Leu Trp Glu Leu Ala Ala Ser Gly Gly Asp Ala
            500                 505                 510

atc ggg ccg ttc ccc acc gac cgc gga tgg ccc acg gaa cag cgt cac   1584
Ile Gly Pro Phe Pro Thr Asp Arg Gly Trp Pro Thr Glu Gln Arg His
        515                 520                 525

gcc cag gac ccc acg cag ccc ggc acg ttc tat ccg cag gga ggc ggg   1632
Ala Gln Asp Pro Thr Gln Pro Gly Thr Phe Tyr Pro Gln Gly Gly Gly
    530                 535                 540

ttc ctt cac gac gcg gcg cac ttc gac gcc ggc ttc ttc gga atc agt   1680
Phe Leu His Asp Ala Ala His Phe Asp Ala Gly Phe Phe Gly Ile Ser
545                 550                 555                 560

cca cgt gag gca ctg gcg atg gat ccg cag cag cgg ctg ctg ctg gag   1728
Pro Arg Glu Ala Leu Ala Met Asp Pro Gln Gln Arg Leu Leu Leu Glu
                565                 570                 575
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acg tcc tgg gag gcg ttc gag cgg gcg gga atc gat ccg ctg tcg gta   1776
Thr Ser Trp Glu Ala Phe Glu Arg Ala Gly Ile Asp Pro Leu Ser Val
            580                 585                 590

cgc ggg tcc cgt acg ggc gtc ttc gcg ggc gcc ctc tcc ttc gac tac   1824
Arg Gly Ser Arg Thr Gly Val Phe Ala Gly Ala Leu Ser Phe Asp Tyr
        595                 600                 605

ggc ccg cgt atg gac acc gcg tcg tcg gag ggc gcc gcg gac gtg gag   1872
Gly Pro Arg Met Asp Thr Ala Ser Ser Glu Gly Ala Ala Asp Val Glu
    610                 615                 620

ggc cac atc ctc acc ggt acc acg ggc agc gtc ctg tcg ggc cgt atc   1920
Gly His Ile Leu Thr Gly Thr Thr Gly Ser Val Leu Ser Gly Arg Ile
625                 630                 635                 640

gcc tac agc ttc ggg ctg gaa ggg ccg gcg atc acc gtg gac acg ggg   1968
Ala Tyr Ser Phe Gly Leu Glu Gly Pro Ala Ile Thr Val Asp Thr Gly
                645                 650                 655

tgc tcg gca tcg ctc gtg acg ctg cat ctg gcg tgc cag tcg ctg cgg   2016
Cys Ser Ala Ser Leu Val Thr Leu His Leu Ala Cys Gln Ser Leu Arg
            660                 665                 670

tcg ggt gag tgc acg ctc gcg ctg gcc ggc ggc gtc tcg gtc atg tcc   2064
Ser Gly Glu Cys Thr Leu Ala Leu Ala Gly Gly Val Ser Val Met Ser
        675                 680                 685

acc ctc ggc atg ttc atc gag ttc tcc cgg cag cgc ggg ctg tcg gtg   2112
Thr Leu Gly Met Phe Ile Glu Phe Ser Arg Gln Arg Gly Leu Ser Val
    690                 695                 700

gac ggc agg tgc aag gcg tac tcg gct gca gcc gac ggc acc ggc tgg   2160
Asp Gly Arg Cys Lys Ala Tyr Ser Ala Ala Ala Asp Gly Thr Gly Trp
705                 710                 715                 720

ggc gag ggc gtc ggg atg ctg ttg gtg gag cgg ttg tcg gat gcg gtg   2208
Gly Glu Gly Val Gly Met Leu Leu Val Glu Arg Leu Ser Asp Ala Val
                725                 730                 735

cgg ctg ggg cat cgg gtg ctg gcg gtg gta cgc ggc agt gcg gtc aac   2256
Arg Leu Gly His Arg Val Leu Ala Val Val Arg Gly Ser Ala Val Asn
            740                 745                 750

cag gac ggt gcg tcg aat ggg ctg acg gcg ccg aac ggt ccg gct cag   2304
Gln Asp Gly Ala Ser Asn Gly Leu Thr Ala Pro Asn Gly Pro Ala Gln
        755                 760                 765

gag cgg gtg atc cgg cag gcg ttg gcg aac gcg ggg ttg tcc gtg gcg   2352
Glu Arg Val Ile Arg Gln Ala Leu Ala Asn Ala Gly Leu Ser Val Ala
    770                 775                 780

gat gtg gat gtg gtg gag ggg cac ggg acg ggc acg acg ctg ggt gat   2400
Asp Val Asp Val Val Glu Gly His Gly Thr Gly Thr Thr Leu Gly Asp
785                 790                 795                 800

ccg atc gag gca cag gcg ttg ctc gcc acg tac ggg cag cgg gcc ggt   2448
Pro Ile Glu Ala Gln Ala Leu Leu Ala Thr Tyr Gly Gln Arg Ala Gly
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gac agg ccg ctg tgg ctg ggg tct ctg aag tcc aac atc ggg cac acc   2496
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            820                 825                 830

atg gct gcc gcg ggt gtg ggt ggg gtc atc aag atg gtg atg gcg ttg   2544
Met Ala Ala Ala Gly Val Gly Gly Val Ile Lys Met Val Met Ala Leu
        835                 840                 845

cgg gag ggg gtg ttg ccg cgg acg ttg cat gtg gat aag ccg tcg ccg   2592
Arg Glu Gly Val Leu Pro Arg Thr Leu His Val Asp Lys Pro Ser Pro
    850                 855                 860

cag gtg gac tgg tcc gcg ggg gcg gtg cgg ctg ctg acg gag gcg gtg   2640
Gln Val Asp Trp Ser Ala Gly Ala Val Arg Leu Leu Thr Glu Ala Val
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ccg tgg ccg ggg gac gcg gca ggg cgg ttg cgg cgg gcg gga gtg tcg   2688
Pro Trp Pro Gly Asp Ala Ala Gly Arg Leu Arg Arg Ala Gly Val Ser
                885                 890                 895

tcg ttc ggg atc ggc ggc acg aat gcg cat gtg att ttg gag gag gcg   2736
Ser Phe Gly Ile Gly Gly Thr Asn Ala His Val Ile Leu Glu Glu Ala
            900                 905                 910

ccg gcg gcg ggg ggc tgt gtt gcc ggg ggt ggg gtg ttg gag ggt gct   2784
Pro Ala Ala Gly Gly Cys Val Ala Gly Gly Gly Val Leu Glu Gly Ala
        915                 920                 925

ccg ggt ctt gcc att tcg gtg gct gag tcg gtg gcc gct cca gtg gct   2832
Pro Gly Leu Ala Ile Ser Val Ala Glu Ser Val Ala Ala Pro Val Ala
    930                 935                 940

gtg tct gcg ccg gtg gct gag tcg gtg ccg gtg ccg gtg ccg gtg ccg   2880
Val Ser Ala Pro Val Ala Glu Ser Val Pro Val Pro Val Pro Val Pro
945                 950                 955                 960

gtt cct gtg ccg gtg tcg gct agg tct gag gct ggg ttg cgg gcg cag   2928
Val Pro Val Pro Val Ser Ala Arg Ser Glu Ala Gly Leu Arg Ala Gln
                965                 970                 975

gcg gag gcg ttg cgt cag tac gtg gca gtc cgg ccg gac gtt tcg ctt   2976
Ala Glu Ala Leu Arg Gln Tyr Val Ala Val Arg Pro Asp Val Ser Leu
            980                 985                 990

gcc gat gtg ggt gcg ggt ctg gcc tgt ggg cgg gct gtg ctg gag cat   3024
Ala Asp Val Gly Ala Gly Leu Ala Cys Gly Arg Ala Val Leu Glu His
        995                1000                1005

cgt gcg gtc gtc ctg gcc gcg gac cgt gag gag ctg gtg caa ggg ttg   3072
Arg Ala Val Val Leu Ala Ala Asp Arg Glu Glu Leu Val Gln Gly Leu
   1010                1015                1020

ggg gcg ctg gcg gcg ggt gag ccg gat cgg cgg gtg acc acg ggt cat   3120
Gly Ala Leu Ala Ala Gly Glu Pro Asp Arg Arg Val Thr Thr Gly His
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gcg ccg ggt ggt gac cgg ggc ggt gtc gtc ttc gtg ttt ccc gga cag   3168
Ala Pro Gly Gly Asp Arg Gly Gly Val Val Phe Val Phe Pro Gly Gln
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Gly Gly Gln Trp Ala Gly Met Gly Val Arg Leu Leu Ala Ser Ser Pro
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gtg ttc gcc cgg cgg atg cag gcg tgc gag gag gct ctg gcg ccg tgg   3264
Val Phe Ala Arg Arg Met Gln Ala Cys Glu Glu Ala Leu Ala Pro Trp
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gtg gac tgg tct gtg gtg gac atc ctg cgc cgg gac gcg ggg gat gcg   3312
Val Asp Trp Ser Val Val Asp Ile Leu Arg Arg Asp Ala Gly Asp Ala
  1090                1095                1100

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Val Trp Glu Arg Ala Asp Val Val Gln Pro Val Leu Phe Ser Val Met
1105                1110                1115                1120

gtg tct ttg gct gct ctg tgg cgt tcc tac ggt atc gaa ccc gac gcg   3408
Val Ser Leu Ala Ala Leu Trp Arg Ser Tyr Gly Ile Glu Pro Asp Ala
              1125                1130                1135

gtc ctt ggc cat tcc cag ggc gag atc gcg gcc gcg cat gtg tgt ggg   3456
Val Leu Gly His Ser Gln Gly Glu Ile Ala Ala Ala His Val Cys Gly
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gcg ctg agc ctg aag gac gcg gcg aag act gtt gcg ctg cgc agc cgg   3504
Ala Leu Ser Leu Lys Asp Ala Ala Lys Thr Val Ala Leu Arg Ser Arg
      1155                1160                1165

gcg ctg gcc gct gtg cgg ggc cgg ggc ggc atg gcc tca gtg ccg ctg   3552
Ala Leu Ala Ala Val Arg Gly Arg Gly Gly Met Ala Ser Val Pro Leu
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cct gcc cag gag gtg gag cag ctc att ggt gag cgg tgg gcg ggg cgg   3600
Pro Ala Gln Glu Val Glu Gln Leu Ile Gly Glu Arg Trp Ala Gly Arg
1185                1190                1195                1200

ttg tgg gtg gcg gcg gtc aac ggc ccc cgc tcc acc gcc gtc tcg ggg   3648
Leu Trp Val Ala Ala Val Asn Gly Pro Arg Ser Thr Ala Val Ser Gly
              1205                1210                1215

gat gcc gag gcg gtg gac gag gtg ctg gcg tac tgt gcc ggc acc ggg   3696
Asp Ala Glu Ala Val Asp Glu Val Leu Ala Tyr Cys Ala Gly Thr Gly
          1220                1225                1230

gtg cgg gcc cgg cgg atc ccg gtc gac tat gcc tcg cac tgc ccc cat   3744
Val Arg Ala Arg Arg Ile Pro Val Asp Tyr Ala Ser His Cys Pro His
      1235                1240                1245

gtg cag ccc ctg cgg gag gag ttg ctg gag ctg ctg ggg gac atc agc   3792
Val Gln Pro Leu Arg Glu Glu Leu Leu Glu Leu Leu Gly Asp Ile Ser
  1250                1255                1260

ccg cag ccg tcc ggc gtg ccg ttc ttc tcc acg gtg gag ggc acc tgg   3840
Pro Gln Pro Ser Gly Val Pro Phe Phe Ser Thr Val Glu Gly Thr Trp
1265                1270                1275                1280

ctg gac acc aca acc ctg gac gcc gcc tac tgg tac cgc aac ctg cac   3888
Leu Asp Thr Thr Thr Leu Asp Ala Ala Tyr Trp Tyr Arg Asn Leu His
              1285                1290                1295
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Replacement Sheet

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Gln Pro Val Arg Phe Ser Asp Ala Val Gln Ala Leu Ala Asp Asp Gly
          1300                1305                1310

cac cgc gtc ttc gtc gaa gtc agc ccc cac ccc acc ctc gtc ccc gcc   3984
His Arg Val Phe Val Glu Val Ser Pro His Pro Thr Leu Val Pro Ala
      1315                1320                1325

atc gaa gac acc acc gaa gac acc gcc gaa gac gtc acc gcg atc ggc   4032
Ile Glu Asp Thr Thr Glu Asp Thr Ala Glu Asp Val Thr Ala Ile Gly
   1330                1335                1340

agc ctc cgc cgc ggc gac aac gac acc cgc cgc ttc ctc acc gcc ctc   4080
Ser Leu Arg Arg Gly Asp Asn Asp Thr Arg Arg Phe Leu Thr Ala Leu
1345                1350                1355                1360

gcc cac acc cat acc acc ggc atc ggc aca ccc acc acc tgg cac cac   4128
Ala His Thr His Thr Thr Gly Ile Gly Thr Pro Thr Thr Trp His His
               1365                1370                1375

cac tac acc cac cac cac acc cac ccc cac ccc cac acg cac ctc gac   4176
His Tyr Thr His His His Thr His Pro His Pro His Thr His Leu Asp
          1380                1385                1390

ctg ccc acc tac ccc ttc caa cac cag cac tac tgg ctc gag agc tca   4224
Leu Pro Thr Tyr Pro Phe Gln His Gln His Tyr Trp Leu Glu Ser Ser
      1395                1400                1405

cag ccg ggt gcc gga tcc ggt tcg ggt gcc ggt gcc ggt tcg ggt gcc   4272
Gln Pro Gly Ala Gly Ser Gly Ser Gly Ala Gly Ala Gly Ser Gly Ala
   1410                1415                1420

ggt tcc ggg cgg gca ggg act gcg ggc ggg acg gca gag gtg gag tcg   4320
Gly Ser Gly Arg Ala Gly Thr Ala Gly Gly Thr Ala Glu Val Glu Ser
1425                1430                1435                1440

cgg ttc tgg gac gcg gtg gcc cgc cag gac ctg gaa acg gtc gcg acc   4368
Arg Phe Trp Asp Ala Val Ala Arg Gln Asp Leu Glu Thr Val Ala Thr
               1445                1450                1455

aca ctc gcc gtg ccc ccc tcc gcc ggc ctg gac acg gtg gtg ccc gca   4416
Thr Leu Ala Val Pro Pro Ser Ala Gly Leu Asp Thr Val Val Pro Ala
          1460                1465                1470

ctc tcc gcc tgg cac cgc cac caa cac gac caa gcc cgc atc aac acc   4464
Leu Ser Ala Trp His Arg His Gln His Asp Gln Ala Arg Ile Asn Thr
      1475                1480                1485

tgg acc tac cag gaa acc tgg aaa ccc ctc acc ctc ccc acc acc cac   4512
Trp Thr Tyr Gln Glu Thr Trp Lys Pro Leu Thr Leu Pro Thr Thr His
   1490                1495                1500

caa ccc cac caa acc tgg ctc atc gcc atc ccc gaa acc cag acc cac   4560
Gln Pro His Gln Thr Trp Leu Ile Ala Ile Pro Glu Thr Gln Thr His
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cac ccc cac atc acc aac atc ctc acc aac ctc cac cac cac ggc atc   4608
His Pro His Ile Thr Asn Ile Leu Thr Asn Leu His His His Gly Ile
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acc ccc atc ccc ctc acc ctc aac cac acc cac acc aac ccc caa cac   4656
Thr Pro Ile Pro Leu Thr Leu Asn His Thr His Thr Asn Pro Gln His
          1540                1545                1550

ctc cac cac acc ctc cac cac acc cga caa caa gcc caa aac cac acc   4704
Leu His His Thr Leu His His Thr Arg Gln Gln Ala Gln Asn His Thr
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acc gga gcc atc acc ggc ctg ctc tcc ctc ctc gcc ctc gac gaa aca   4752
Thr Gly Ala Ile Thr Gly Leu Leu Ser Leu Leu Ala Leu Asp Glu Thr
   1570                1575                1580

ccc cac ccc cac cac ccc cac aca ccc acc ggc acc ctc ctc aac ctc   4800
Pro His Pro His His Pro His Thr Pro Thr Gly Thr Leu Leu Asn Leu
1585                1590                1595                1600

acc ctc acc caa acc cac acc caa acc cac cca cca acc ccc ctc tgg   4848
Thr Leu Thr Gln Thr His Thr Gln Thr His Pro Pro Thr Pro Leu Trp
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tac gcc acc acc aac gcc acc acc acc cac ccc aac gac ccc ctc aca   4896
Tyr Ala Thr Thr Asn Ala Thr Thr Thr His Pro Asn Asp Pro Leu Thr
          1620                1625                1630

cac ccc acc caa gcc caa acc tgg gga ctc gcc cgc acc acc ctc ctc   4944
His Pro Thr Gln Ala Gln Thr Trp Gly Leu Ala Arg Thr Thr Leu Leu
       1635                1640                1645

gaa cac ccc acc cac acc gcc gga atc atc gac ctc ccc acc acc ccc   4992
Glu His Pro Thr His Thr Ala Gly Ile Ile Asp Leu Pro Thr Thr Pro
   1650                1655                1660

acc ccc cac acc ctc cag cac ctc acc caa acc ctc acc caa ccc cac   5040
Thr Pro His Thr Leu Gln His Leu Thr Gln Thr Leu Thr Gln Pro His
1665                1670                1675                1680

cac caa acc caa ctc gcc atc cgc acc acc ggc acc cac acc cgc cgc   5088
His Gln Thr Gln Leu Ala Ile Arg Thr Thr Gly Thr His Thr Arg Arg
               1685                1690                1695

ctc acc ccc acc acc ctc acc ccc aca cac caa cca ccc acc ccc acc   5136
Leu Thr Pro Thr Thr Leu Thr Pro Thr His Gln Pro Pro Thr Pro Thr
          1700                1705                1710

ccc cac gga acc acc ctc atc acc ggc gga acc ggc gcc ctc gcc acc   5184
Pro His Gly Thr Thr Leu Ile Thr Gly Gly Thr Gly Ala Leu Ala Thr
       1715                1720                1725

cac ctc acc cac cac ctc acc acc cac caa ccc acc caa cac ctc ctc   5232
His Leu Thr His His Leu Thr Thr His Gln Pro Thr Gln His Leu Leu
   1730                1735                1740

ctc acc agc cga acc ggc ccc cac acc ccc cac gca caa cac ctc acc   5280
Leu Thr Ser Arg Thr Gly Pro His Thr Pro His Ala Gln His Leu Thr
1745                1750                1755                1760

acc caa ctc caa caa aaa ggc atc cac ctc acc atc acc acc tgc gac   5328
Thr Gln Leu Gln Gln Lys Gly Ile His Leu Thr Ile Thr Thr Cys Asp
               1765                1770                1775
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acc agc aac cca gac caa ctc caa caa ctc ctc aac acc atc ccc cca   5376
Thr Ser Asn Pro Asp Gln Leu Gln Gln Leu Leu Asn Thr Ile Pro Pro
          1780                1785                1790

caa cac ccc ctc acc acc gtc atc cac acc gca ggc atc ctc gac gac   5424
Gln His Pro Leu Thr Thr Val Ile His Thr Ala Gly Ile Leu Asp Asp
      1795                1800                1805

gcc acc ctc acc aac ctc acc ccc acc caa ctc aac aac gtc ctc cgc   5472
Ala Thr Leu Thr Asn Leu Thr Pro Thr Gln Leu Asn Asn Val Leu Arg
  1810                1815                1820

gcc aaa gcc cac agc gcc cac ctc ctc cac caa ctc acc caa cac acc   5520
Ala Lys Ala His Ser Ala His Leu Leu His Gln Leu Thr Gln His Thr
1825                1830                1835                1840

ccc ctc acc gcc ttc gtc ctc tac tcc tcc gcc gcc gcc acc ttc ggc   5568
Pro Leu Thr Ala Phe Val Leu Tyr Ser Ser Ala Ala Ala Thr Phe Gly
              1845                1850                1855

gca ccc ggc caa gcc aac tac gcc gca gcc aac gcc tac ctc gac gcc   5616
Ala Pro Gly Gln Ala Asn Tyr Ala Ala Ala Asn Ala Tyr Leu Asp Ala
          1860                1865                1870

ctc gcc cac cac cgc cac acc cac cac ctc ccc gcc acc agc atc gcc   5664
Leu Ala His His Arg His Thr His His Leu Pro Ala Thr Ser Ile Ala
      1875                1880                1885

tgg ggc acc tgg caa gga aac gga ctc gct gat tcg gac aag gcc cgc   5712
Trp Gly Thr Trp Gln Gly Asn Gly Leu Ala Asp Ser Asp Lys Ala Arg
  1890                1895                1900

gca tat ctc gac cgc cgc ggg ttt cga ccc atg tca ccc gag ttg gcc   5760
Ala Tyr Leu Asp Arg Arg Gly Phe Arg Pro Met Ser Pro Glu Leu Ala
1905                1910                1915                1920

acg gca gcg gtc acg cag gcg atc gcg gac acc gaa cgg ccg tat gtc   5808
Thr Ala Ala Val Thr Gln Ala Ile Ala Asp Thr Glu Arg Pro Tyr Val
              1925                1930                1935

gtc atc gcc gac atc gac tgg agc aag atc gaa cac acc tct cag acc   5856
Val Ile Ala Asp Ile Asp Trp Ser Lys Ile Glu His Thr Ser Gln Thr
          1940                1945                1950

agc gac ctg gtg agc gcg gcc cgg gaa agg gag cca gct gtc cag cgc   5904
Ser Asp Leu Val Ser Ala Ala Arg Glu Arg Glu Pro Ala Val Gln Arg
      1955                1960                1965

ccc act cca ccg gcg gag ttg cac aaa acg ctg gcc cat cag acg tcg   5952
Pro Thr Pro Pro Ala Glu Leu His Lys Thr Leu Ala His Gln Thr Ser
  1970                1975                1980

gcc gac caa cgg gcc gca ttg ctc gag ctc gta cga gac cat gtg gcg   6000
Ala Asp Gln Arg Ala Ala Leu Leu Glu Leu Val Arg Asp His Val Ala
1985                1990                1995                2000

gca gtg ctc cgg cac gcg gac ccg aaa gcc atc gcg ccc gac cag tcg   6048
Ala Val Leu Arg His Ala Asp Pro Lys Ala Ile Ala Pro Asp Gln Ser
              2005                2010                2015
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ttc cgt gca ctc ggc ttc gat tca ctc acg gcc gtc gag ttc cga aac   6096
Phe Arg Ala Leu Gly Phe Asp Ser Leu Thr Ala Val Glu Phe Arg Asn
          2020                2025                2030

ctg ctg atc aag gca aca gga ctc cgc ctt cct gtc tcg ctg gtc ttc   6144
Leu Leu Ile Lys Ala Thr Gly Leu Arg Leu Pro Val Ser Leu Val Phe
       2035                2040                2045

gac cac ccg acc cct gcc aaa ctc gcc gta cac ctg cag aac caa ctg   6192
Asp His Pro Thr Pro Ala Lys Leu Ala Val His Leu Gln Asn Gln Leu
   2050                2055                2060

cgg ggc aca gca gcg gag tcg gct cct tca gcg gca gcc gtt acc gcc   6240
Arg Gly Thr Ala Ala Glu Ser Ala Pro Ser Ala Ala Ala Val Thr Ala
2065                2070                2075                2080

gag gct tct gtc acc gag ccg atc gcc atc gtt ggc atg gcc tgt cgt   6288
Glu Ala Ser Val Thr Glu Pro Ile Ala Ile Val Gly Met Ala Cys Arg
               2085                2090                2095

ttc ccc ggc gga gtg acc tcg gcg gac gac ttc tgg gat ctg atc tcc   6336
Phe Pro Gly Gly Val Thr Ser Ala Asp Asp Phe Trp Asp Leu Ile Ser
          2100                2105                2110

tcc gag cag gac gcg atc ggc gga ttc ccc acc gac cgc ggc tgg gac   6384
Ser Glu Gln Asp Ala Ile Gly Gly Phe Pro Thr Asp Arg Gly Trp Asp
       2115                2120                2125

ctg gac acg ctc tac gac ccc gac ccc gac cac ccc ggc acc tgc tac   6432
Leu Asp Thr Leu Tyr Asp Pro Asp Pro Asp His Pro Gly Thr Cys Tyr
   2130                2135                2140

acc cga aac ggc gga ttc ctc tac gac gca ggc cac ttc gac gcc gaa   6480
Thr Arg Asn Gly Gly Phe Leu Tyr Asp Ala Gly His Phe Asp Ala Glu
2145                2150                2155                2160

ttc ttc ggc atc agc ccc cgc gaa gcc ctc gcc atg gac ccc cag caa   6528
Phe Phe Gly Ile Ser Pro Arg Glu Ala Leu Ala Met Asp Pro Gln Gln
               2165                2170                2175

cga ctc ctc ctc gaa acc gcc tgg gaa acc atc gaa cac gcc ggc atc   6576
Arg Leu Leu Leu Glu Thr Ala Trp Glu Thr Ile Glu His Ala Gly Ile
          2180                2185                2190

aac ccc cac acc ctc cac ggc acc ccc acc gga gtc ttc acc ggc acc   6624
Asn Pro His Thr Leu His Gly Thr Pro Thr Gly Val Phe Thr Gly Thr
       2195                2200                2205

aac gga cag gac tac gca ctt cgc gtg cac aac gcg ggc cag tca acc   6672
Asn Gly Gln Asp Tyr Ala Leu Arg Val His Asn Ala Gly Gln Ser Thr
   2210                2215                2220

gat ggt ttc gca ctg acc gga acc gcc ggc agc gtc atc tcc ggt cgt   6720
Asp Gly Phe Ala Leu Thr Gly Thr Ala Gly Ser Val Ile Ser Gly Arg
2225                2230                2235                2240

atc tcg tac acg ttt ggt ttt gag ggt cct gcg gtg tcg gtg gac acg   6768
Ile Ser Tyr Thr Phe Gly Phe Glu Gly Pro Ala Val Ser Val Asp Thr
               2245                2250                2255
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gct tgt tcc tcg tcg ttg gtg gct ttg cat ctg gcc tgt cag gcg ttg   6816
Ala Cys Ser Ser Ser Leu Val Ala Leu His Leu Ala Cys Gln Ala Leu
          2260                2265                2270

cgt gcg ggt gag tgc tcg atg gcg ctt gcc ggg ggt gtg acg gtg atg   6864
Arg Ala Gly Glu Cys Ser Met Ala Leu Ala Gly Gly Val Thr Val Met
      2275                2280                2285

tcg tct ccg ggt gcc ttc gtg gag ttt tcg cgg cag cgg ggt ctg gcc   6912
Ser Ser Pro Gly Ala Phe Val Glu Phe Ser Arg Gln Arg Gly Leu Ala
  2290                2295                2300

gcg gac ggg cat tgc aag gcg ttc tcg gcg gcg gcg gac ggg acc ggc   6960
Ala Asp Gly His Cys Lys Ala Phe Ser Ala Ala Ala Asp Gly Thr Gly
2305                2310                2315                2320

tgg ggt gag ggt gtg ggg atg ctg ctg gtg gag cgg ctc tcc gac gcc   7008
Trp Gly Glu Gly Val Gly Met Leu Leu Val Glu Arg Leu Ser Asp Ala
               2325                2330                2335

cat cgc aac ggt cac cgt gtc ctg gcc gtg gtg cgt ggc agt gcg gtc   7056
His Arg Asn Gly His Arg Val Leu Ala Val Val Arg Gly Ser Ala Val
          2340                2345                2350

aac cag gac ggt gcg agc aac ggt ctg acc gcg ccc aac ggg ccg tcc   7104
Asn Gln Asp Gly Ala Ser Asn Gly Leu Thr Ala Pro Asn Gly Pro Ser
      2355                2360                2365

cag cag cgt gtc atc cgc cag gcc ctc gcc aac gcc ggc ttg tcg gcc   7152
Gln Gln Arg Val Ile Arg Gln Ala Leu Ala Asn Ala Gly Leu Ser Ala
  2370                2375                2380

ggt gat gtc gac gcg gtg gag gcc cac ggc acc ggc acc act ttg ggc   7200
Gly Asp Val Asp Ala Val Glu Ala His Gly Thr Gly Thr Thr Leu Gly
2385                2390                2395                2400

gac ccg atc gag gcc cag gcc ctc ctc gcg acc tac gga cag gac cgt   7248
Asp Pro Ile Glu Ala Gln Ala Leu Leu Ala Thr Tyr Gly Gln Asp Arg
               2405                2410                2415

gcc ggc gag ggg ccg ctg tgg ctg ggc tcg gtc aag tcc aat gtc ggt   7296
Ala Gly Glu Gly Pro Leu Trp Leu Gly Ser Val Lys Ser Asn Val Gly
          2420                2425                2430

cac aca cag gct gcc gcg ggc gtc gcc ggg gtg atc aag atg gtg atg   7344
His Thr Gln Ala Ala Ala Gly Val Ala Gly Val Ile Lys Met Val Met
      2435                2440                2445

gcg ctg cgg cat ggt ctg ctg ccg cgg acg ttg cat gtg gat gag ccg   7392
Ala Leu Arg His Gly Leu Leu Pro Arg Thr Leu His Val Asp Glu Pro
  2450                2455                2460

tcg ccg cat gtg gac tgg tcc gcg ggt gcg gtg cag ctg ctg acg gag   7440
Ser Pro His Val Asp Trp Ser Ala Gly Ala Val Gln Leu Leu Thr Glu
2465                2470                2475                2480

acg gtg ccc tgg ccc ggc ggg gag ggg cgg cta cgg cgg gca gga gtg   7488
Thr Val Pro Trp Pro Gly Gly Glu Gly Arg Leu Arg Arg Ala Gly Val
               2485                2490                2495
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tca tca ttc ggc gtc agc ggc acc aac gcc cac gtc atc ctc gaa gaa   7536
Ser Ser Phe Gly Val Ser Gly Thr Asn Ala His Val Ile Leu Glu Glu
          2500                2505                2510

gca ccc gcc gac gac gtt ccg ggg gga cca ccc gcc ggc gag ggt gac   7584
Ala Pro Ala Asp Asp Val Pro Gly Gly Pro Pro Ala Gly Glu Gly Asp
       2515                2520                2525

gcg ggc agc gac gat gag gct gct gcc ggc agt cct ggg gtg tgg ccg   7632
Ala Gly Ser Asp Asp Glu Ala Ala Ala Gly Ser Pro Gly Val Trp Pro
   2530                2535                2540

tgg ctg gtg tcg gcc aag tcg cag ccg gcc ctg cgc gcc cag gcc cag   7680
Trp Leu Val Ser Ala Lys Ser Gln Pro Ala Leu Arg Ala Gln Ala Gln
2545                2550                2555                2560

gcc ctg cac gcc cac ctc acc gac cac ccc ggc ctc gac ctc gcg gat   7728
Ala Leu His Ala His Leu Thr Asp His Pro Gly Leu Asp Leu Ala Asp
               2565                2570                2575

gtc gga tac acc ctc gcc cac gcc cgc gcc gtg ttc gac cac cgc gcc   7776
Val Gly Tyr Thr Leu Ala His Ala Arg Ala Val Phe Asp His Arg Ala
          2580                2585                2590

acc ctc atc gcc gcg gac cgc gac acg ttc ctg caa gca ctc cag gca   7824
Thr Leu Ile Ala Ala Asp Arg Asp Thr Phe Leu Gln Ala Leu Gln Ala
       2595                2600                2605

ctc gcc gca ggc gag ccc cac ccc gcc gtc atc cac agc agc gcc ccg   7872
Leu Ala Ala Gly Glu Pro His Pro Ala Val Ile His Ser Ser Ala Pro
   2610                2615                2620

ggc ggg acc ggg acc ggg gag gcc gca gga aag acc gca ttc atc tgc   7920
Gly Gly Thr Gly Thr Gly Glu Ala Ala Gly Lys Thr Ala Phe Ile Cys
2625                2630                2635                2640

tcc gga cag ggc acc caa cgc ccc ggc atg gcc cac ggc ctc tac cac   7968
Ser Gly Gln Gly Thr Gln Arg Pro Gly Met Ala His Gly Leu Tyr His
               2645                2650                2655

acc cac ccc gtc ttc gcc gcc gca ctc aac gac atc tgc acc cac ctc   8016
Thr His Pro Val Phe Ala Ala Ala Leu Asn Asp Ile Cys Thr His Leu
          2660                2665                2670

gac ccc cac ctc gac cac ccc ctc ctc ccc ctc ctc acc caa aac gac   8064
Asp Pro His Leu Asp His Pro Leu Leu Pro Leu Leu Thr Gln Asn Asp
       2675                2680                2685

aac gac aac gag gac gcg gcc gca ctg ctc cag cag acc cgc tac gcc   8112
Asn Asp Asn Glu Asp Ala Ala Ala Leu Leu Gln Gln Thr Arg Tyr Ala
   2690                2695                2700

cag ccc gcc ctc ttc gcc ttc cag gtc gcc ctc cac cgc ctc ctc acc   8160
Gln Pro Ala Leu Phe Ala Phe Gln Val Ala Leu His Arg Leu Leu Thr
2705                2710                2715                2720

gac ggc tac cac atc acc ccc cac tac tac gcc gga cac tcc ctc ggc   8208
Asp Gly Tyr His Ile Thr Pro His Tyr Tyr Ala Gly His Ser Leu Gly
               2725                2730                2735
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gaa atc acc gcc gcc cac ctc gcc ggc atc ctc acc ctc acc gac gcc   8256
Glu Ile Thr Ala Ala His Leu Ala Gly Ile Leu Thr Leu Thr Asp Ala
          2740                2745                2750

acc acc ctc atc acc caa cgc gcc acc ctc atg caa acc atg ccc ccc   8304
Thr Thr Leu Ile Thr Gln Arg Ala Thr Leu Met Gln Thr Met Pro Pro
      2755                2760                2765

ggc acc atg acc acc ctc cac acc acc ccc cac cac atc acc cac cac   8352
Gly Thr Met Thr Thr Leu His Thr Thr Pro His His Ile Thr His His
   2770                2775                2780

ctc acc gcc cac gaa aac gac ctc gcc atc gcc gcc atc aac acc ccc   8400
Leu Thr Ala His Glu Asn Asp Leu Ala Ile Ala Ala Ile Asn Thr Pro
2785                2790                2795                2800

acc tcc ctc gtc atc agc ggc acc ccc cac acc gtc caa cac atc acc   8448
Thr Ser Leu Val Ile Ser Gly Thr Pro His Thr Val Gln His Ile Thr
               2805                2810                2815

acc ctc tgc caa caa caa ggc atc aaa acc aaa acc ctc ccc acc aac   8496
Thr Leu Cys Gln Gln Gln Gly Ile Lys Thr Lys Thr Leu Pro Thr Asn
          2820                2825                2830

cac gcc ttc cac tcc ccc cac acc aac ccc atc ctc aac caa ctc cac   8544
His Ala Phe His Ser Pro His Thr Asn Pro Ile Leu Asn Gln Leu His
      2835                2840                2845

cag cac acc caa acc ctc acc tac cac cca ccc cac acc ccc ctc atc   8592
Gln His Thr Gln Thr Leu Thr Tyr His Pro Pro His Thr Pro Leu Ile
   2850                2855                2860

acc gcc aac acc cca ccc gac caa ctc ctc acc ccc cac tac tgg acc   8640
Thr Ala Asn Thr Pro Pro Asp Gln Leu Leu Thr Pro His Tyr Trp Thr
2865                2870                2875                2880

caa caa gcc cgc aac acc gtc gac tac gcc acc acc acc caa acc ctc   8688
Gln Gln Ala Arg Asn Thr Val Asp Tyr Ala Thr Thr Thr Gln Thr Leu
               2885                2890                2895

cac caa cac ggc gtc acc acc tac atc gaa ctc gga ccc gac aac acc   8736
His Gln His Gly Val Thr Thr Tyr Ile Glu Leu Gly Pro Asp Asn Thr
          2900                2905                2910

ctc acc acc ctc acc cac cac aac ctc ccc aac ccc ccc acc acc acc   8784
Leu Thr Thr Leu Thr His His Asn Leu Pro Asn Pro Pro Thr Thr Thr
      2915                2920                2925

ctc acc ctc acc cac ccc cac cac cac ccc caa acc cac ctc ctc acc   8832
Leu Thr Leu Thr His Pro His His His Pro Gln Thr His Leu Leu Thr
   2930                2935                2940

aac ctc gcc aaa acc acc acc acc tgg cac ccc cac cac tac acc cac   8880
Asn Leu Ala Lys Thr Thr Thr Thr Trp His Pro His His Tyr Thr His
2945                2950                2955                2960

cac gac aac caa ccc cac acc cac acc cac ctc gac ctc ccc acc tac   8928
His Asp Asn Gln Pro His Thr His Thr His Leu Asp Leu Pro Thr Tyr
               2965                2970                2975
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ccc ttc caa cac cac cac tac tgg ctc gaa agc aca cag ccc ggt gcc   8976
Pro Phe Gln His His His Tyr Trp Leu Glu Ser Thr Gln Pro Gly Ala
          2980                2985                2990

ggc aac gtg tca gca gcc gga ctc gac ccc acc gaa cac ccc cta ctc   9024
Gly Asn Val Ser Ala Ala Gly Leu Asp Pro Thr Glu His Pro Leu Leu
       2995                3000                3005

ggc gcc aca ttg gaa ctg gcg act gac ggt gga gcg ctt ctt gca ggg   9072
Gly Ala Thr Leu Glu Leu Ala Thr Asp Gly Gly Ala Leu Leu Ala Gly
   3010                3015                3020

cgc ttg tct ttg agg tcg cat ccg tgg ctg gct gac cat gcc gtc ggc   9120
Arg Leu Ser Leu Arg Ser His Pro Trp Leu Ala Asp His Ala Val Gly
3025                3030                3035                3040

ggc acg gtg ctg ctg tcg ggc gcc acc ttc ctc gaa ctc gcc ctt cat   9168
Gly Thr Val Leu Leu Ser Gly Ala Thr Phe Leu Glu Leu Ala Leu His
               3045                3050                3055

gcg ggc aca tac gtg ggc tgc gac cga gtg gat gag ctg acg ctg cat   9216
Ala Gly Thr Tyr Val Gly Cys Asp Arg Val Asp Glu Leu Thr Leu His
          3060                3065                3070

gcg ccg ctg gtg gtt cct gtg gat ggg ggt gtg agt gtg cag gtt ggg   9264
Ala Pro Leu Val Val Pro Val Asp Gly Gly Val Ser Val Gln Val Gly
       3075                3080                3085

gtt gcg gct gcg gat ggg gag ggg cgg cgt ttg gtg agt gtg tat gcg   9312
Val Ala Ala Ala Asp Gly Glu Gly Arg Arg Leu Val Ser Val Tyr Ala
   3090                3095                3100

cgg ggt ggg agt gct tgt ggt ggg ggt ggt gcg tcg ggt ggg gtg tgg   9360
Arg Gly Gly Ser Ala Cys Gly Gly Gly Gly Ala Ser Gly Gly Val Trp
3105                3110                3115                3120

acg tgt cat gcc tcg ggg gtg ctg gtt gag gct gct gct ggt ggt gtg   9408
Thr Cys His Ala Ser Gly Val Leu Val Glu Ala Ala Ala Gly Gly Val
               3125                3130                3135

gtg gtg gat ggt ctg gcg ggg gtg tgg ccg ccg cgg ggt gcg gtg gcg   9456
Val Val Asp Gly Leu Ala Gly Val Trp Pro Pro Arg Gly Ala Val Ala
          3140                3145                3150

gtg gat gtc gat ggt gtc cgt gac cgt ttg gct ggg gct ggt tgt gtt   9504
Val Asp Val Asp Gly Val Arg Asp Arg Leu Ala Gly Ala Gly Cys Val
       3155                3160                3165

ttg ggg ccg gtg ttt tcg ggg ctg cgt gcg gtg tgg cgt gat ggg ggg   9552
Leu Gly Pro Val Phe Ser Gly Leu Arg Ala Val Trp Arg Asp Gly Gly
   3170                3175                3180

gat ttg ctg gct gag gtg tgt ctg ccg gag gag gcg tgg ggt gat gcg   9600
Asp Leu Leu Ala Glu Val Cys Leu Pro Glu Glu Ala Trp Gly Asp Ala
3185                3190                3195                3200

gct ggt ttt ggg ctg cat ccg gcg ttg ctg gat ggt gtg gtc cag ccg   9648
Ala Gly Phe Gly Leu His Pro Ala Leu Leu Asp Gly Val Val Gln Pro
               3205                3210                3215
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ttg tcg gtg ttg ctt ccg ggt ggg acg ggg ttt ggg gag ggg gcg ggg   9696
Leu Ser Val Leu Leu Pro Gly Gly Thr Gly Phe Gly Glu Gly Ala Gly
          3220                3225                3230

ttc ggg gag ggt gtt cgg gtg ccg gct gtg tgg ggt ggt gtg tcg ctt   9744
Phe Gly Glu Gly Val Arg Val Pro Ala Val Trp Gly Gly Val Ser Leu
       3235                3240                3245

cac cgg gcg ggt gtg acc ggt gtg cgg gtg cgt gtg tcg gct gtc ggg   9792
His Arg Ala Gly Val Thr Gly Val Arg Val Arg Val Ser Ala Val Gly
   3250                3255                3260

cgg ggc ggc ggg cgt gag gcg gtg tcg gtc gtg gtc ggg gat gag gcg   9840
Arg Gly Gly Gly Arg Glu Ala Val Ser Val Val Val Gly Asp Glu Ala
3265                3270                3275                3280

ggt gtg ccg gtg gcg tcg gtc gat cgt ctt gag ttg cgg cct gtg gat   9888
Gly Val Pro Val Ala Ser Val Asp Arg Leu Glu Leu Arg Pro Val Asp
               3285                3290                3295

atg ggt cag ttg cgt gct gtc tcg gtt tcg gcg ggg cgg cgg ggt tcg   9936
Met Gly Gln Leu Arg Ala Val Ser Val Ser Ala Gly Arg Arg Gly Ser
          3300                3305                3310

ctg tat gcg gtg cag tgg gct gag gtg ggt cct gtg ccg gtg tgt ggg   9984
Leu Tyr Ala Val Gln Trp Ala Glu Val Gly Pro Val Pro Val Cys Gly
       3315                3320                3325

cag gcg tgg gcg tgg cac gag gac gtg ggt gag agc ggt ggt ggg cct   10032
Gln Ala Trp Ala Trp His Glu Asp Val Gly Glu Ser Gly Gly Gly Pro
   3330                3335                3340

gtg ccg ggg gtg gtg gtg ttg cgg tgc ccg gat gcc ggt gcc ggt ggc   10080
Val Pro Gly Val Val Val Leu Arg Cys Pro Asp Ala Gly Ala Gly Gly
3345                3350                3355                3360

ggt ggc ggt ggc ggt ggt ggc ggt ggt gtg ggt gag gtt gtt ggt ggg   10128
Gly Gly Gly Gly Gly Gly Gly Gly Gly Val Gly Glu Val Val Gly Gly
               3365                3370                3375

gtg ttg ggt gtg gtg cag ggg tgg ctg ggg ctg gag cgg ttt gcg ggt   10176
Val Leu Gly Val Val Gln Gly Trp Leu Gly Leu Glu Arg Phe Ala Gly
          3380                3385                3390

tcg cgg ctg gtg gtg gtg acc cgg ggt gcg gtg gtg gcc ggc ccg gag   10224
Ser Arg Leu Val Val Val Thr Arg Gly Ala Val Val Ala Gly Pro Glu
       3395                3400                3405

gac ggc ccg gtg gat gtg gtg ggt gcg tcg gtg tgg ggg ctg gtg cgt   10272
Asp Gly Pro Val Asp Val Val Gly Ala Ser Val Trp Gly Leu Val Arg
   3410                3415                3420

tcg gcg cag gct gag cat ccg gac cgg ttt gtc ctc ctc gac ctc gac   10320
Ser Ala Gln Ala Glu His Pro Asp Arg Phe Val Leu Leu Asp Leu Asp
3425                3430                3435                3440

acc gac acc ggc acc gac ctc gac acc ggt gct ggt gct ggt tgg ggc   10368
Thr Asp Thr Gly Thr Asp Leu Asp Thr Gly Ala Gly Ala Gly Trp Gly
               3445                3450                3455
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gtg gat ggt ggg cgt gtg gcg gcg gtg gtg gcg tgt ggt gag ccg cag   10416
Val Asp Gly Gly Arg Val Ala Ala Val Val Ala Cys Gly Glu Pro Gln
          3460                3465                3470

ttg gcg gtg cgt ggg gag cgg ttg ctg gcc gca cgc ctg aaa cga ctt   10464
Leu Ala Val Arg Gly Glu Arg Leu Leu Ala Ala Arg Leu Lys Arg Leu
       3475                3480                3485

gag tca tcc ggt gat gtt cca gcc cag cgg tcc ggt gac aca cga gcc   10512
Glu Ser Ser Gly Asp Val Pro Ala Gln Arg Ser Gly Asp Thr Arg Ala
   3490                3495                3500

cgg cgg tcc gac gtg cct gcc cag cgc tcc ggt ggc gtg cct gct cgg   10560
Arg Arg Ser Asp Val Pro Ala Gln Arg Ser Gly Gly Val Pro Ala Arg
3505                3510                3515                3520

cgg tcg gtt gat gta tcg ggt cgg gag gtg ttg ccg tgg ttg tcg ggt   10608
Arg Ser Val Asp Val Ser Gly Arg Glu Val Leu Pro Trp Leu Ser Gly
               3525                3530                3535

ggg tcg gtg ttg gtg acg ggt ggg acg ggt gtg ctg ggt gcg gcg gtg   10656
Gly Ser Val Leu Val Thr Gly Gly Thr Gly Val Leu Gly Ala Ala Val
          3540                3545                3550

gcg cgg cat ctg gct ggt gtg tgt ggg gtg cgg gat ctg ctg ttg gtg   10704
Ala Arg His Leu Ala Gly Val Cys Gly Val Arg Asp Leu Leu Leu Val
       3555                3560                3565

agc cgg cgt ggt ccg gat gct ccg ggt gcg gag ggt ctg cgg gcg gag   10752
Ser Arg Arg Gly Pro Asp Ala Pro Gly Ala Glu Gly Leu Arg Ala Glu
   3570                3575                3580

ctg gcc gcg ttg ggg gcg gag gtg cgg att gtt gcg tgt gat gtg ggg   10800
Leu Ala Ala Leu Gly Ala Glu Val Arg Ile Val Ala Cys Asp Val Gly
3585                3590                3595                3600

gag cgg cgg gag gtg gtc cgg ctg ctg gag ggt gtt cct gcc ggg tgt   10848
Glu Arg Arg Glu Val Val Arg Leu Leu Glu Gly Val Pro Ala Gly Cys
               3605                3610                3615

ccg ctg acg ggt gtc gtg cat gcg gct ggt gtg ctg gac gat gcg acg   10896
Pro Leu Thr Gly Val Val His Ala Ala Gly Val Leu Asp Asp Ala Thr
          3620                3625                3630

atc gcc tct ctc acg ccc gag cgg ctg ggc acg gtg ttc gcg gcc aag   10944
Ile Ala Ser Leu Thr Pro Glu Arg Leu Gly Thr Val Phe Ala Ala Lys
       3635                3640                3645

gtg gat gcc gct ctt ttg ctg gat gag ctg acg cgg ggt atg gag ctg   10992
Val Asp Ala Ala Leu Leu Leu Asp Glu Leu Thr Arg Gly Met Glu Leu
   3650                3655                3660

tcg gcg ttc gtg ctg ttc tcc tcg gcc gcg ggg atc ctg ggg tcg gcc   11040
Ser Ala Phe Val Leu Phe Ser Ser Ala Ala Gly Ile Leu Gly Ser Ala
3665                3670                3675                3680

ggg cag ggc aac tac gcc gcg gcc aat gcc gct ctg gac gcg ctg gcg   11088
Gly Gln Gly Asn Tyr Ala Ala Ala Asn Ala Ala Leu Asp Ala Leu Ala
               3685                3690                3695
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tac cgg cgg cgg gcg gcg ggt ctg ccg ggg gtg tcg ctg gcg tgg ggg   11136
Tyr Arg Arg Arg Ala Ala Gly Leu Pro Gly Val Ser Leu Ala Trp Gly
          3700                3705                3710

ctg tgg gaa gag gcc agc ggg atg acc ggg cac ctg gcc ggc acc gac   11184
Leu Trp Glu Glu Ala Ser Gly Met Thr Gly His Leu Ala Gly Thr Asp
       3715                3720                3725

cac cgg cgc atc atc cgt tcc ggt ctg cat ccc atg tcg acc ccg gac   11232
His Arg Arg Ile Ile Arg Ser Gly Leu His Pro Met Ser Thr Pro Asp
   3730                3735                3740

gca ctg gcc ctc ttc gat gcg gcc ctg gct ctg gac cgg ccg gtc ctg   11280
Ala Leu Ala Leu Phe Asp Ala Ala Leu Ala Leu Asp Arg Pro Val Leu
3745                3750                3755                3760

ctg ccc gcc gac ctg cgt ccc gcc ccg ccc ctg ccg ccc ctg ctg cag   11328
Leu Pro Ala Asp Leu Arg Pro Ala Pro Pro Leu Pro Pro Leu Leu Gln
               3765                3770                3775

gac ctc ctg ccc gcc acc cgc cgc cgc acc acc cgc acc acc act acc   11376
Asp Leu Leu Pro Ala Thr Arg Arg Arg Thr Thr Arg Thr Thr Thr Thr
          3780                3785                3790

ggt ggt gcg gac aac ggc gcc cag ctg cac gcc cgg ctg gcc ggc cag   11424
Gly Gly Ala Asp Asn Gly Ala Gln Leu His Ala Arg Leu Ala Gly Gln
       3795                3800                3805

aca cac gaa caa cag cac acc acc ctc ctc gcc ctg gtc cgc tcc cac   11472
Thr His Glu Gln Gln His Thr Thr Leu Leu Ala Leu Val Arg Ser His
   3810                3815                3820

atc gcc acc gtc ctg ggc cac acc acc ccc gac acc atc ccc ccc gac   11520
Ile Ala Thr Val Leu Gly His Thr Thr Pro Asp Thr Ile Pro Pro Asp
3825                3830                3835                3840

cgc gcg ttc cgc gac ctc ggc ttc gac tcc ctc acc gcc gtc gaa cta   11568
Arg Ala Phe Arg Asp Leu Gly Phe Asp Ser Leu Thr Ala Val Glu Leu
               3845                3850                3855

cgc aac cgg ctc tcc cgc acc acc gga ctc cgc ctc ccc acc acc ctc   11616
Arg Asn Arg Leu Ser Arg Thr Thr Gly Leu Arg Leu Pro Thr Thr Leu
          3860                3865                3870

gcc ttc gac cac ccc aac ccc acc acc ctc acc cac cac ctc cac aca   11664
Ala Phe Asp His Pro Asn Pro Thr Thr Leu Thr His His Leu His Thr
       3875                3880                3885

caa ctc cag cca caa ccg gac aac gct gtc gcc ccc gtg ttg gcg gag   11712
Gln Leu Gln Pro Gln Pro Asp Asn Ala Val Ala Pro Val Leu Ala Glu
   3890                3895                3900

ctc gac aaa ctc gaa tcc gcc ctc tcc gcc ctc gac aaa acc gac agc   11760
Leu Asp Lys Leu Glu Ser Ala Leu Ser Ala Leu Asp Lys Thr Asp Ser
3905                3910                3915                3920

gcc agc gaa aga gtc acc ctg cgg ctg aag tca ctc atg ttg agg tgg   11808
Ala Ser Glu Arg Val Thr Leu Arg Leu Lys Ser Leu Met Leu Arg Trp
               3925                3930                3935
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aac gca ccc cag cat ccg aca gcc gaa agc gct gat gac gac gag aag 11856
Asn Ala Pro Gln His Pro Thr Ala Glu Ser Ala Asp Asp Asp Glu Lys
3940 3945 3950

ttc aca tcg gca aca gag gct gag att ttc aaa ttc att gac aac gac 11904
Phe Thr Ser Ala Thr Glu Ala Glu Ile Phe Lys Phe Ile Asp Asn Asp
3955 3960 3965

ctc ggc ctg tcc tgaaccggac gcctgccact ccgcccgtat ccgctgggcc 11956
Leu Gly Leu Ser
3970

ctgctaggac gtga atg caa ttg gcg aat gaa gcg aag ctc ctg gaa tac 12006
Met Gln Leu Ala Asn Glu Ala Lys Leu Leu Glu Tyr
3975 3980

ctc aag cgc gtc act gcg gac ctg gac cgc act cgc cgt cgc ctg tac 12054
Leu Lys Arg Val Thr Ala Asp Leu Asp Arg Thr Arg Arg Arg Leu Tyr
3985 3990 3995 4000

gag gtg gtc gag cgt gag cag gag ccg atc gcg att gtg ggg atg gcg 12102
Glu Val Val Glu Arg Glu Gln Glu Pro Ile Ala Ile Val Gly Met Ala
4005 4010 4015

tgt cgt tac cca ggc ggg gcg acg tca ccc acg cga ctg tgg cat ctc 12150
Cys Arg Tyr Pro Gly Gly Ala Thr Ser Pro Thr Arg Leu Trp His Leu
4020 4025 4030

gtc aag tcc cag acg gac gct atc ggg gag ttc ccg acc gac cgt gga 12198
Val Lys Ser Gln Thr Asp Ala Ile Gly Glu Phe Pro Thr Asp Arg Gly
4035 4040 4045

tgg aac ctg gag cag ctc tac gac ccg gac ccc gac cgc tca gga acc 12246
Trp Asn Leu Glu Gln Leu Tyr Asp Pro Asp Pro Asp Arg Ser Gly Thr
4050 4055 4060

agt tac acg cgc agc gga ggg ttt ctc tat gac gcg ggc gac ttc gac 12294
Ser Tyr Thr Arg Ser Gly Gly Phe Leu Tyr Asp Ala Gly Asp Phe Asp
4065 4070 4075 4080

gcc gcg ttc ttc gag ttg tca ccg cgt gag gcg ctg gca atg gac ccg 12342
Ala Ala Phe Phe Glu Leu Ser Pro Arg Glu Ala Leu Ala Met Asp Pro
4085 4090 4095

cag cag cgc ctg ctg ctc gaa acc act tgg gaa acg ttc gaa cag ggc 12390
Gln Gln Arg Leu Leu Leu Glu Thr Thr Trp Glu Thr Phe Glu Gln Gly
4100 4105 4110

gga atc gac ccg agg tcc atg cgc gga agc cgg acc ggg gtt ttc gtg 12438
Gly Ile Asp Pro Arg Ser Met Arg Gly Ser Arg Thr Gly Val Phe Val
4115 4120 4125

ggg atc aat ccg gag gac tac acc acc gga tac aca cat cag ccc tca 12486
Gly Ile Asn Pro Glu Asp Tyr Thr Thr Gly Tyr Thr His Gln Pro Ser
4130 4135 4140

aac gca gtc gag ggc tac ctg ctc act ggc agc gcg gca agc att gcg 12534
Asn Ala Val Glu Gly Tyr Leu Leu Thr Gly Ser Ala Ala Ser Ile Ala
4145 4150 4155 4160

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tca ggc cgt atc tcc tac aac ttc ggg ctc gaa ggc cct gcg atc act   12582
Ser Gly Arg Ile Ser Tyr Asn Phe Gly Leu Glu Gly Pro Ala Ile Thr
                4165                4170                4175

atc gac acc gcg tgt tcc tcc tcg ctc gtc gcc ctg cat ctg gcc tgc   12630
Ile Asp Thr Ala Cys Ser Ser Ser Leu Val Ala Leu His Leu Ala Cys
            4180                4185                4190

caa gcg ctc cgg tcc ggt gaa tgc acc atg gcg ctc gca ggc ggc gcc   12678
Gln Ala Leu Arg Ser Gly Glu Cys Thr Met Ala Leu Ala Gly Gly Ala
        4195                4200                4205

tcc gtc atg gcc act ccc ttc gtc ttc acc gag ttc tct cgc cag cgg   12726
Ser Val Met Ala Thr Pro Phe Val Phe Thr Glu Phe Ser Arg Gln Arg
    4210                4215                4220

ggc ctg gcc gca gac ggc cgg tgc aag gcg ttt tcg gcg gcg gcg gac   12774
Gly Leu Ala Ala Asp Gly Arg Cys Lys Ala Phe Ser Ala Ala Ala Asp
4225                4230                4235                4240

ggg acc ggc tgg tcc gag ggt gtg ggg atg ctg ctg gtg gag cgg ctc   12822
Gly Thr Gly Trp Ser Glu Gly Val Gly Met Leu Leu Val Glu Arg Leu
                4245                4250                4255

tcc gac gcc cgc cgc aac ggt cac cgt gtc ctg gcc gtc gtc cgc ggc   12870
Ser Asp Ala Arg Arg Asn Gly His Arg Val Leu Ala Val Val Arg Gly
            4260                4265                4270

agc gcc gtc aac cag gac ggc gca agc aac ggc ctg acc gca ccc aac   12918
Ser Ala Val Asn Gln Asp Gly Ala Ser Asn Gly Leu Thr Ala Pro Asn
        4275                4280                4285

ggt cgt tca caa gtc aag gtc atc cgc cag gct ttg gcc aac gca cac   12966
Gly Arg Ser Gln Val Lys Val Ile Arg Gln Ala Leu Ala Asn Ala His
    4290                4295                4300

ctc tcc cct gcc gat gtc gat gcg gtg gag gcc cac ggc acg ggg acc   13014
Leu Ser Pro Ala Asp Val Asp Ala Val Glu Ala His Gly Thr Gly Thr
4305                4310                4315                4320

acc ctg ggc gac ccg atc gag gct caa gcc ctc gtc gaa gcc tac ggt   13062
Thr Leu Gly Asp Pro Ile Glu Ala Gln Ala Leu Val Glu Ala Tyr Gly
                4325                4330                4335

cag gac cgc ccc aac ggc cgc ccc ctc tgg ctc gga acc ctc aag tcc   13110
Gln Asp Arg Pro Asn Gly Arg Pro Leu Trp Leu Gly Thr Leu Lys Ser
            4340                4345                4350

aac atc ggg cac tcc atg gcc gct gcg ggt gtg ggc ggg gtc atc aag   13158
Asn Ile Gly His Ser Met Ala Ala Ala Gly Val Gly Gly Val Ile Lys
        4355                4360                4365

atg gtg atg gcg ctg cgg aat ggt ctg ctg ccg cgg acg ttg cat gtg   13206
Met Val Met Ala Leu Arg Asn Gly Leu Leu Pro Arg Thr Leu His Val
    4370                4375                4380

gat gag ccg tcg ccg cat gtg gac tgg tcc gcg ggt gcg gtg cag ctg   13254
Asp Glu Pro Ser Pro His Val Asp Trp Ser Ala Gly Ala Val Gln Leu
4385                4390                4395                4400
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ctg acg gag acg gtg ccc tgg ccc ggc ggg gag ggg cgg cta cgg cgg   13302
Leu Thr Glu Thr Val Pro Trp Pro Gly Gly Glu Gly Arg Leu Arg Arg
                4405                4410                4415

gca gga gtg tca tca ttc ggc gtc agc ggc acc aac gcc cac gtc atc   13350
Ala Gly Val Ser Ser Phe Gly Val Ser Gly Thr Asn Ala His Val Ile
            4420                4425                4430

ctc gag gaa gca ccc gcc cac aac atc ccg tca gac aca ccc gcc gac   13398
Leu Glu Glu Ala Pro Ala His Asn Ile Pro Ser Asp Thr Pro Ala Asp
        4435                4440                4445

gac gtc ccg gga gaa tca gcc gcc gac gag gat gcc ggt agt ggc gat   13446
Asp Val Pro Gly Glu Ser Ala Ala Asp Glu Asp Ala Gly Ser Gly Asp
    4450                4455                4460

gag gct gct gcc ggc agt cca ggg gtg tgg ccg tgg ctg gtg tcg gcc   13494
Glu Ala Ala Ala Gly Ser Pro Gly Val Trp Pro Trp Leu Val Ser Ala
4465                4470                4475                4480

aag tcg cag ccg gcc ctg cgc gcc cag gcc cag gcc ctg cac gcc cac   13542
Lys Ser Gln Pro Ala Leu Arg Ala Gln Ala Gln Ala Leu His Ala His
                4485                4490                4495

ctc acc gac cac ccc ggc ctc gac ctc gcc gac gtc ggg tac acc ctc   13590
Leu Thr Asp His Pro Gly Leu Asp Leu Ala Asp Val Gly Tyr Thr Leu
            4500                4505                4510

gcc cac gcc cgc gcc gtg ttc gac cac cgc gcc acc ctc atc gcc gcc   13638
Ala His Ala Arg Ala Val Phe Asp His Arg Ala Thr Leu Ile Ala Ala
        4515                4520                4525

gac cgc gac acc ttc ctg caa gca ctc cag gca ctc gcc gca ggc gaa   13686
Asp Arg Asp Thr Phe Leu Gln Ala Leu Gln Ala Leu Ala Ala Gly Glu
    4530                4535                4540

ccc cac ccc gcc gtc atc cac agc agc gcc cca ggc ggg acc ggg acc   13734
Pro His Pro Ala Val Ile His Ser Ser Ala Pro Gly Gly Thr Gly Thr
4545                4550                4555                4560

ggg gag gcc gca gga aag acc gca ttc atc tgc tcc gga cag ggc acc   13782
Gly Glu Ala Ala Gly Lys Thr Ala Phe Ile Cys Ser Gly Gln Gly Thr
                4565                4570                4575

caa cgc ccc ggc atg gcc cac ggc ctc tac cac acc cac ccc gtc ttc   13830
Gln Arg Pro Gly Met Ala His Gly Leu Tyr His Thr His Pro Val Phe
            4580                4585                4590

gcc gcc gca ctc aac gac atc tgc acc cac ctc gac ccc cac ctc gac   13878
Ala Ala Ala Leu Asn Asp Ile Cys Thr His Leu Asp Pro His Leu Asp
        4595                4600                4605

cac ccc ctc ctc ccc ctc ctc acc cag gac ccc aac acc cag gac acc   13926
His Pro Leu Leu Pro Leu Leu Thr Gln Asp Pro Asn Thr Gln Asp Thr
    4610                4615                4620

acc acc ctc gaa gaa gcg gcc gca ctg ctc cag cag acc cgc tac gcc   13974
Thr Thr Leu Glu Glu Ala Ala Ala Leu Leu Gln Gln Thr Arg Tyr Ala
4625                4630                4635                4640
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cag ccc gcc ctc ttc gcc ttc cag gtc gcc ctc cac cgc ctc ctc acc   14022
Gln Pro Ala Leu Phe Ala Phe Gln Val Ala Leu His Arg Leu Leu Thr
               4645                4650                4655

gac ggc tac cac atc acc ccc cac tac tac gcc gga cac tcc ctc ggc   14070
Asp Gly Tyr His Ile Thr Pro His Tyr Tyr Ala Gly His Ser Leu Gly
           4660                4665                4670

gaa atc acc gcc gcc cac ctc gcc ggc atc ctc acc ctc acc gac gcc   14118
Glu Ile Thr Ala Ala His Leu Ala Gly Ile Leu Thr Leu Thr Asp Ala
       4675                4680                4685

acc acc ctc atc acc caa cgc gcc acc ctc atg caa acc atg ccc ccc   14166
Thr Thr Leu Ile Thr Gln Arg Ala Thr Leu Met Gln Thr Met Pro Pro
   4690                4695                4700

ggc acc atg acc acc ctc cac acc acc ccc cac cac atc acc cac cac   14214
Gly Thr Met Thr Thr Leu His Thr Thr Pro His His Ile Thr His His
4705                4710                4715                4720

ctc acc gcc cac gaa aac gac ctc gcc atc gcc gcc atc aac acc ccc   14262
Leu Thr Ala His Glu Asn Asp Leu Ala Ile Ala Ala Ile Asn Thr Pro
               4725                4730                4735

acc tcc ctc gtc atc agc ggc acc ccc cac acc gtc caa cac atc acc   14310
Thr Ser Leu Val Ile Ser Gly Thr Pro His Thr Val Gln His Ile Thr
           4740                4745                4750

acc ctc tgc caa caa caa ggc atc aaa acc aaa acc ctc ccc acc aac   14358
Thr Leu Cys Gln Gln Gln Gly Ile Lys Thr Lys Thr Leu Pro Thr Asn
       4755                4760                4765

cac gcc ttc cac tcc ccc cac acc aac ccc atc ctc aac caa ctc cac   14406
His Ala Phe His Ser Pro His Thr Asn Pro Ile Leu Asn Gln Leu His
   4770                4775                4780

cag cac acc caa acc ctc acc tac cac cca ccc cac acc ccc ctc atc   14454
Gln His Thr Gln Thr Leu Thr Tyr His Pro Pro His Thr Pro Leu Ile
4785                4790                4795                4800

acc gcc aac acc cca ccc gac caa ctc ctc acc ccc cac tac tgg acc   14502
Thr Ala Asn Thr Pro Pro Asp Gln Leu Leu Thr Pro His Tyr Trp Thr
               4805                4810                4815

caa caa gcc cgc aac acc gtc gac tac gcc acc acc acc caa acc ctc   14550
Gln Gln Ala Arg Asn Thr Val Asp Tyr Ala Thr Thr Thr Gln Thr Leu
           4820                4825                4830

cac caa cac ggc gtc acc acc tac atc gaa ctc gga ccc gac aac acc   14598
His Gln His Gly Val Thr Thr Tyr Ile Glu Leu Gly Pro Asp Asn Thr
       4835                4840                4845

ctc acc acc ctc acc cac gac aac ctc ccc aac acc ccc acc acc acc   14646
Leu Thr Thr Leu Thr His Asp Asn Leu Pro Asn Thr Pro Thr Thr Thr
   4850                4855                4860

ctc acc ctc acc cac ccc cac cac cac ccc caa acc cac ctc ctc acc   14694
Leu Thr Leu Thr His Pro His His His Pro Gln Thr His Leu Leu Thr
4865                4870                4875                4880
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aac ctc gcc aaa acc acc acc acc tgg cac ccc cac cac tac acc cac   14742
Asn Leu Ala Lys Thr Thr Thr Thr Trp His Pro His His Tyr Thr His
                4885                4890                4895

cac cac aac caa ccc cac acc cac acc cac ctc gac ctc ccc acc tac   14790
His His Asn Gln Pro His Thr His Thr His Leu Asp Leu Pro Thr Tyr
            4900                4905                4910

ccc ttc caa cac cac cac tac tgg ctc caa cca ccc ggc aag ccg agc   14838
Pro Phe Gln His His His Tyr Trp Leu Gln Pro Pro Gly Lys Pro Ser
        4915                4920                4925

gac ccg tca ccg agc gaa ggc cgt gag caa gcc acg acc cca tca acc   14886
Asp Pro Ser Pro Ser Glu Gly Arg Glu Gln Ala Thr Thr Pro Ser Thr
    4930                4935                4940

ccg ctg cgt gat gtc ctc gtg ggc aag tct ccg cag gag cga gac gaa   14934
Pro Leu Arg Asp Val Leu Val Gly Lys Ser Pro Gln Glu Arg Asp Glu
4945                4950                4955                4960

gag ctg ttg cgc ctg gtg cgc acc cat gcg gcc gct gtg ctg ggc cat   14982
Glu Leu Leu Arg Leu Val Arg Thr His Ala Ala Ala Val Leu Gly His
                4965                4970                4975

gcc act ccc gaa gtg atc gtt ccg aac aag gcc ttc aaa gag ctg ggt   15030
Ala Thr Pro Glu Val Ile Val Pro Asn Lys Ala Phe Lys Glu Leu Gly
            4980                4985                4990

ttt gat tct ctc gcc gca att cag ctt cgt aat cga ctg ctt gct gac   15078
Phe Asp Ser Leu Ala Ala Ile Gln Leu Arg Asn Arg Leu Leu Ala Asp
        4995                5000                5005

gtt gac ctg ccg ctt ccg gcc acg ctg atc ttc gat tac ccc act ccg   15126
Val Asp Leu Pro Leu Pro Ala Thr Leu Ile Phe Asp Tyr Pro Thr Pro
    5010                5015                5020

atg gcg ctt tgc cag ttc ctc cgg gcg gcg atc gtc gga gcg gac aca   15174
Met Ala Leu Cys Gln Phe Leu Arg Ala Ala Ile Val Gly Ala Asp Thr
5025                5030                5035                5040

ggc acg acc act cgt ctg ccg cta act gcg gtc ccc gcc gac gag ccg   15222
Gly Thr Thr Thr Arg Leu Pro Leu Thr Ala Val Pro Ala Asp Glu Pro
                5045                5050                5055

atc gcc atc gtc ggc atg gcc tgt cgg tac ccc ggt gat gta cgg acg   15270
Ile Ala Ile Val Gly Met Ala Cys Arg Tyr Pro Gly Asp Val Arg Thr
            5060                5065                5070

gtc gat gat ctc tgg cag gtg gtc agt ggt ggc cat gac gcg atc ggc   15318
Val Asp Asp Leu Trp Gln Val Val Ser Gly Gly His Asp Ala Ile Gly
        5075                5080                5085

gga ttc ccg acg aac cgt ggg tgg gac ctc gac acg ctg tac aac ccg   15366
Gly Phe Pro Thr Asn Arg Gly Trp Asp Leu Asp Thr Leu Tyr Asn Pro
    5090                5095                5100

gac ccg gac cac cac gga acc agc tac acc cgg agc ggc gga ttc ctt   15414
Asp Pro Asp His His Gly Thr Ser Tyr Thr Arg Ser Gly Gly Phe Leu
5105                5110                5115                5120
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tac gac gca ggc aat ttc gat ccc gac ttc ttc ggt atc agt ccg cgt   15462
Tyr Asp Ala Gly Asn Phe Asp Pro Asp Phe Phe Gly Ile Ser Pro Arg
               5125                5130                5135

gag gca ctg gcg atg gac ccg cag cag cgg ctg ctg ctg gaa aca gcg   15510
Glu Ala Leu Ala Met Asp Pro Gln Gln Arg Leu Leu Leu Glu Thr Ala
           5140                5145                5150

tgg gag agc atc gaa cac gcc tgc atc aac ccc gac agc ctc cgt ggc   15558
Trp Glu Ser Ile Glu His Ala Cys Ile Asn Pro Asp Ser Leu Arg Gly
       5155                5160                5165

aca cca acc ggc gtc ttc gcc ggg ctg acc tac cac gac tac gcc gcg   15606
Thr Pro Thr Gly Val Phe Ala Gly Leu Thr Tyr His Asp Tyr Ala Ala
   5170                5175                5180

cgc ttt ccc aca gct ccg gca ggg ttc gag ggg tat ctc ggg cac gga   15654
Arg Phe Pro Thr Ala Pro Ala Gly Phe Glu Gly Tyr Leu Gly His Gly
5185                5190                5195                5200

agc gca ggc agt atc gcc tcg ggt cgt gtc gcc tac gct ctc ggc ctg   15702
Ser Ala Gly Ser Ile Ala Ser Gly Arg Val Ala Tyr Ala Leu Gly Leu
               5205                5210                5215

gaa ggt ccg gcc ctc aca gtc gac act gcc tgc tct tcg tcc ctg gtc   15750
Glu Gly Pro Ala Leu Thr Val Asp Thr Ala Cys Ser Ser Ser Leu Val
           5220                5225                5230

gct ctg cac ctg gcc tgt cag gcg ctg cgg tcc ggc gag tgt tcc atg   15798
Ala Leu His Leu Ala Cys Gln Ala Leu Arg Ser Gly Glu Cys Ser Met
       5235                5240                5245

gcc ctc gcg ggt ggc gtc acg gtg atg tca acc ccg gcc ggg ttc gtg   15846
Ala Leu Ala Gly Gly Val Thr Val Met Ser Thr Pro Ala Gly Phe Val
   5250                5255                5260

gag ttt tcg cgg cag cgg ggc ctg gcc gtg gac ggg cgg tgc aag gcg   15894
Glu Phe Ser Arg Gln Arg Gly Leu Ala Val Asp Gly Arg Cys Lys Ala
5265                5270                5275                5280

ttc tcg gca gcg gct gac ggc acc ggc tgg ggt gag ggt gtc gga atg   15942
Phe Ser Ala Ala Ala Asp Gly Thr Gly Trp Gly Glu Gly Val Gly Met
               5285                5290                5295

ctg ctg gtg gag cgg ctg tcg gac gcg cgg cgg ctc ggt cac cga atc   15990
Leu Leu Val Glu Arg Leu Ser Asp Ala Arg Arg Leu Gly His Arg Ile
           5300                5305                5310

ctc gcg gtg gtg cgt ggc agt gcg gtc aat cag gac ggt gcg agc aac   16038
Leu Ala Val Val Arg Gly Ser Ala Val Asn Gln Asp Gly Ala Ser Asn
       5315                5320                5325

ggg ctg acg gcg ccc aac ggg ccg tcc cag gag cgt gtc atc cgc ctg   16086
Gly Leu Thr Ala Pro Asn Gly Pro Ser Gln Glu Arg Val Ile Arg Leu
   5330                5335                5340

gcc ctg gcc aac gcg gac ctg acc ccc gcc gac gtc gat gcg gtg gag   16134
Ala Leu Ala Asn Ala Asp Leu Thr Pro Ala Asp Val Asp Ala Val Glu
5345                5350                5355                5360
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gcc cac ggc acc ggc acc act ttg ggc gac ccg atc gag gcc cag gcc   16182
Ala His Gly Thr Gly Thr Thr Leu Gly Asp Pro Ile Glu Ala Gln Ala
               5365                5370                5375

ctc ctc gcc acc tac gga cag gac cgc ccc ggc aac gaa ccg ctg tgg   16230
Leu Leu Ala Thr Tyr Gly Gln Asp Arg Pro Gly Asn Glu Pro Leu Trp
           5380                5385                5390

ctg ggc tcg atg aag tcg aac atc ggc cac gcg cag gct gcc gca ggt   16278
Leu Gly Ser Met Lys Ser Asn Ile Gly His Ala Gln Ala Ala Ala Gly
       5395                5400                5405

gtg ggc ggg gtc atc aag atg gtg atg gcg ctg cgg aat ggt ctg ctg   16326
Val Gly Gly Val Ile Lys Met Val Met Ala Leu Arg Asn Gly Leu Leu
   5410                5415                5420

ccg cgg acg ttg cat gtg gat gag ccg tcg ccg cat gtg gac tgg tcc   16374
Pro Arg Thr Leu His Val Asp Glu Pro Ser Pro His Val Asp Trp Ser
5425                5430                5435                5440

gcg ggg gcg gtg cag ctg ctg acg gag acg gtg ccc tgg ccc ggc ggg   16422
Ala Gly Ala Val Gln Leu Leu Thr Glu Thr Val Pro Trp Pro Gly Gly
               5445                5450                5455

gag ggg cgg ctg cgg cgg gca gga gtg tca tcg ttc ggc gtc agc ggc   16470
Glu Gly Arg Leu Arg Arg Ala Gly Val Ser Ser Phe Gly Val Ser Gly
           5460                5465                5470

acc aac gcc cac gtc atc ctc gaa gaa gca ccc gcc cac aac atc ccg   16518
Thr Asn Ala His Val Ile Leu Glu Glu Ala Pro Ala His Asn Ile Pro
       5475                5480                5485

tca gac aca ccc gcc gac gac gcc ccg gga gaa gca gcc gcc gac gat   16566
Ser Asp Thr Pro Ala Asp Asp Ala Pro Gly Glu Ala Ala Ala Asp Asp
   5490                5495                5500

gtt ccg ggg gaa gcg gcc ggc gac gac gcc ggt acc ggc ggg gaa gcg   16614
Val Pro Gly Glu Ala Ala Gly Asp Asp Ala Gly Thr Gly Gly Glu Ala
5505                5510                5515                5520

act ggt cct gct gcc ggc agt cca ggg gtg tgg ccg tgg ctg gtg tcg   16662
Thr Gly Pro Ala Ala Gly Ser Pro Gly Val Trp Pro Trp Leu Val Ser
               5525                5530                5535

gcc aag tcg cag ccg gcc ctg cgc gcc cag gcc cag gcc ctg cac gcc   16710
Ala Lys Ser Gln Pro Ala Leu Arg Ala Gln Ala Gln Ala Leu His Ala
           5540                5545                5550

cac ctc acc gac cac ccc ggc ctc gac ctc gcc gac gtc ggg tac acc   16758
His Leu Thr Asp His Pro Gly Leu Asp Leu Ala Asp Val Gly Tyr Thr
       5555                5560                5565

ctc gcc cac gcc cgc gcc gtg ttc gac cac cgc gcc acc ctc atc gcc   16806
Leu Ala His Ala Arg Ala Val Phe Asp His Arg Ala Thr Leu Ile Ala
   5570                5575                5580

gcc gac cgc gac acc ttc ctg caa gca ctc cag gca ctc gcc gca ggc   16854
Ala Asp Arg Asp Thr Phe Leu Gln Ala Leu Gln Ala Leu Ala Ala Gly
5585                5590                5595                5600
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gaa ccc cac ccc gcc gtc atc cac agc agc gcc cca ggc ggg acc ggg 16902
Glu Pro His Pro Ala Val Ile His Ser Ser Ala Pro Gly Gly Thr Gly
5605 5610 5615

acc ggg gag gcc gca gga aag acc gca ttc atc tgc tcc gga cag ggc 16950
Thr Gly Glu Ala Ala Gly Lys Thr Ala Phe Ile Cys Ser Gly Gln Gly
5620 5625 5630

acc caa cgc ccc ggc atg gcc cac ggc ctc tac cac acc cac ccc gtc 16998
Thr Gln Arg Pro Gly Met Ala His Gly Leu Tyr His Thr His Pro Val
5635 5640 5645

ttc gcc gcc gca ctc aac gac atc tgc acc cac ctc gac ccc cac ctc 17046
Phe Ala Ala Ala Leu Asn Asp Ile Cys Thr His Leu Asp Pro His Leu
5650 5655 5660

gac cac ccc ctc ctc ccc ctc ctc acc cag gac ccc aac acc cag gac 17094
Asp His Pro Leu Leu Pro Leu Leu Thr Gln Asp Pro Asn Thr Gln Asp
5665 5670 5675 5680

acc acc acc ctc gaa gaa gcg gcc gca ctg ctc cag cag acc ccg tac 17142
Thr Thr Thr Leu Glu Glu Ala Ala Ala Leu Leu Gln Gln Thr Pro Tyr
5685 5690 5695

gcc cag ccc gcc ctc ttc gcc ttc cag gtc gcc ctc cac cgc ctc ctc 17190
Ala Gln Pro Ala Leu Phe Ala Phe Gln Val Ala Leu His Arg Leu Leu
5700 5705 5710

acc gac ggc tac cac atc acc ccc cac tac tac gcc gga cac tcc ctc 17238
Thr Asp Gly Tyr His Ile Thr Pro His Tyr Tyr Ala Gly His Ser Leu
5715 5720 5725

ggc gaa atc acc gcc gcc cac ctc gcc ggc atc ctc acc ctc acc gac 17286
Gly Glu Ile Thr Ala Ala His Leu Ala Gly Ile Leu Thr Leu Thr Asp
5730 5735 5740

gcc acc acc ctc atc acc caa cgc gcc acc ctc atg caa acc atg ccc 17334
Ala Thr Thr Leu Ile Thr Gln Arg Ala Thr Leu Met Gln Thr Met Pro
5745 5750 5755 5760

ccc ggc acc atg acc acc ctc cac acc acc ccc cac cac atc acc cac 17382
Pro Gly Thr Met Thr Thr Leu His Thr Thr Pro His His Ile Thr His
5765 5770 5775

cac ctc acc gcc cac gaa aac gac ctc gcc atc gcc gcc atc aac acc 17430
His Leu Thr Ala His Glu Asn Asp Leu Ala Ile Ala Ala Ile Asn Thr
5780 5785 5790

ccc acc tcc ctc gtc atc agc ggc acc ccc cac acc gtc caa cac atc 17478
Pro Thr Ser Leu Val Ile Ser Gly Thr Pro His Thr Val Gln His Ile
5795 5800 5805

acc acc ctc tgc caa caa caa ggc atc aaa acc aaa acc ctc ccc acc 17526
Thr Thr Leu Cys Gln Gln Gln Gly Ile Lys Thr Lys Thr Leu Pro Thr
5810 5815 5820

aaa aac gcc ttc cac tcc ccc cac acc aac ccc atc ctc aac caa ctc 17574
Lys Asn Ala Phe His Ser Pro His Thr Asn Pro Ile Leu Asn Gln Leu
5825 5830 5835 5840

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cac cag cac acc caa acc ctc acc tac cac cca ccc cac acc ccc ctc   17622
His Gln His Thr Gln Thr Leu Thr Tyr His Pro Pro His Thr Pro Leu
               5845                5850                5855

atc acc gcc aac acc cca ccc gac caa ctc ctc acc ccc cac tac tgg   17670
Ile Thr Ala Asn Thr Pro Pro Asp Gln Leu Leu Thr Pro His Tyr Trp
           5860                5865                5870

acc caa caa gcc cgc aac acc gtc gac tac gcc acc acc acc caa acc   17718
Thr Gln Gln Ala Arg Asn Thr Val Asp Tyr Ala Thr Thr Thr Gln Thr
       5875                5880                5885

ctc cac caa cac ggc gtc acc acc tac atc gaa ctc gga ccc gac aac   17766
Leu His Gln His Gly Val Thr Thr Tyr Ile Glu Leu Gly Pro Asp Asn
   5890                5895                5900

acc ctc acc acc ctc acc cac cac aac ctc ccc aac acc ccc acc acc   17814
Thr Leu Thr Thr Leu Thr His His Asn Leu Pro Asn Thr Pro Thr Thr
5905                5910                5915                5920

acc ctc acc ctc acc cac ccc cac cac cac ccc caa acc cac ctc ctc   17862
Thr Leu Thr Leu Thr His Pro His His His Pro Gln Thr His Leu Leu
               5925                5930                5935

acc aac ctc gcc aaa acc acc acc acc tgg cac ccc cac cac tac acc   17910
Thr Asn Leu Ala Lys Thr Thr Thr Thr Trp His Pro His His Tyr Thr
           5940                5945                5950

cac cac cac aac caa ccc cac acc cac acc cac ctc gac ctc ccc acc   17958
His His His Asn Gln Pro His Thr His Thr His Leu Asp Leu Pro Thr
       5955                5960                5965

tac ccc ttc caa cac cag cac tac tgg ctc gaa agc aca cag ccg ggt   18006
Tyr Pro Phe Gln His Gln His Tyr Trp Leu Glu Ser Thr Gln Pro Gly
   5970                5975                5980

gcc gga tcc ggt tcg ggt tcc ggt tcc ggg cgg gca ggg act gcg ggc   18054
Ala Gly Ser Gly Ser Gly Ser Gly Ser Gly Arg Ala Gly Thr Ala Gly
5985                5990                5995                6000

ggg acg gca gag gtg gag tcg cgg ttc tgg gac gcg gtg gcc cgc cag   18102
Gly Thr Ala Glu Val Glu Ser Arg Phe Trp Asp Ala Val Ala Arg Gln
               6005                6010                6015

gac ctg gaa acg gtc gcg acc acg ctc gcc gtg ccc ccc tcc gcc ggc   18150
Asp Leu Glu Thr Val Ala Thr Thr Leu Ala Val Pro Pro Ser Ala Gly
           6020                6025                6030

ctg gac acg gtg gtg ccc gca ctc tcc gcc tgg cac cgc cac caa cac   18198
Leu Asp Thr Val Val Pro Ala Leu Ser Ala Trp His Arg His Gln His
       6035                6040                6045

gac caa gcc cgc atc aac acc tgg acc tac cag gaa acc tgg aaa ccc   18246
Asp Gln Ala Arg Ile Asn Thr Trp Thr Tyr Gln Glu Thr Trp Lys Pro
   6050                6055                6060

ctc acc ctc ccc acc acc cac caa ccc cac caa acc tgg ctc atc gcc   18294
Leu Thr Leu Pro Thr Thr His Gln Pro His Gln Thr Trp Leu Ile Ala
6065                6070                6075                6080
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atc ccc gaa acc cag acc cac cac ccc cac atc acc aac atc ctc acc   18342
Ile Pro Glu Thr Gln Thr His His Pro His Ile Thr Asn Ile Leu Thr
                6085                6090                6095

aac ctc cac cac cac ggc atc acc ccc atc ccc ctc acc ctc aac cac   18390
Asn Leu His His His Gly Ile Thr Pro Ile Pro Leu Thr Leu Asn His
            6100                6105                6110

acc cac acc aac ccc caa cac ctc cac cac acc cga caa caa gcc caa   18438
Thr His Thr Asn Pro Gln His Leu His His Thr Arg Gln Gln Ala Gln
        6115                6120                6125

aac cac acc acc gga ccc atc acc ggc ctg ctc tcc ctc ctc gcc ctc   18486
Asn His Thr Thr Gly Pro Ile Thr Gly Leu Leu Ser Leu Leu Ala Leu
    6130                6135                6140

gac gaa aca ccc cac ccc cac cac ccc cac aca ccc acc ggc acc ctc   18534
Asp Glu Thr Pro His Pro His His Pro His Thr Pro Thr Gly Thr Leu
6145                6150                6155                6160

ctc aac ctc acc ctc acc caa acc cac acc caa acc cac cca cca acc   18582
Leu Asn Leu Thr Leu Thr Gln Thr His Thr Gln Thr His Pro Pro Thr
                6165                6170                6175

ccc ctc tgg tac gcc acc acc aac gcc acc acc acc cac ccc aac gac   18630
Pro Leu Trp Tyr Ala Thr Thr Asn Ala Thr Thr Thr His Pro Asn Asp
            6180                6185                6190

ccc ctc aca cac ccc acc caa gcc caa acc tgg gga ctc gcc cgc acc   18678
Pro Leu Thr His Pro Thr Gln Ala Gln Thr Trp Gly Leu Ala Arg Thr
        6195                6200                6205

acc ctc ctc gaa cac ccc acc cac acc gcc gga atc atc gac ctc ccc   18726
Thr Leu Leu Glu His Pro Thr His Thr Ala Gly Ile Ile Asp Leu Pro
    6210                6215                6220

acc acc ccc acc ccc cac acc ctc cac cac ctc acc caa acc ctc acc   18774
Thr Thr Pro Thr Pro His Thr Leu His His Leu Thr Gln Thr Leu Thr
6225                6230                6235                6240

caa ccc cac cac caa acc caa ctc gcc atc cgc acc acc ggc acc cac   18822
Gln Pro His His Gln Thr Gln Leu Ala Ile Arg Thr Thr Gly Thr His
                6245                6250                6255

acc cgc cgc ctc acc ccc acc acc ctc acc ccc aca cac caa cca ccc   18870
Thr Arg Arg Leu Thr Pro Thr Thr Leu Thr Pro Thr His Gln Pro Pro
            6260                6265                6270

acc ccc acc ccc cac gga acc acc ctc atc acc ggc gga acc ggc gcc   18918
Thr Pro Thr Pro His Gly Thr Thr Leu Ile Thr Gly Gly Thr Gly Ala
        6275                6280                6285

ctc gcc acc cac ctc acc cac cac ctc acc acc cac caa ccc acc caa   18966
Leu Ala Thr His Leu Thr His His Leu Thr Thr His Gln Pro Thr Gln
    6290                6295                6300

cac ctc ctc ctc acc agc cga acc ggc ccc cac acc ccc cac gca caa   19014
His Leu Leu Leu Thr Ser Arg Thr Gly Pro His Thr Pro His Ala Gln
6305                6310                6315                6320
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cac ctc acc acc caa ctc caa caa aaa ggc atc cac ctc acc atc acc   19062
His Leu Thr Thr Gln Leu Gln Gln Lys Gly Ile His Leu Thr Ile Thr
               6325                6330                6335

acc tgc gac acc agc aac cca gac caa ctc caa caa ctc ctc aac acc   19110
Thr Cys Asp Thr Ser Asn Pro Asp Gln Leu Gln Gln Leu Leu Asn Thr
           6340                6345                6350

atc ccc cca caa cac ccc ctc acc acc gtc atc cac acc gca ggc atc   19158
Ile Pro Pro Gln His Pro Leu Thr Thr Val Ile His Thr Ala Gly Ile
       6355                6360                6365

ctc gac gac gcc acc ctc acc aac ctc acc ccc acc caa ctc aac aac   19206
Leu Asp Asp Ala Thr Leu Thr Asn Leu Thr Pro Thr Gln Leu Asn Asn
   6370                6375                6380

gtc ctc cgc gcc aaa gcc cac agc gcc cac ctc ctc cac caa ctc acc   19254
Val Leu Arg Ala Lys Ala His Ser Ala His Leu Leu His Gln Leu Thr
6385                6390                6395                6400

caa cac acc ccc ctc aac gcc ttc gtc ctc tac tcc tcc gcc gcc gcc   19302
Gln His Thr Pro Leu Asn Ala Phe Val Leu Tyr Ser Ser Ala Ala Ala
               6405                6410                6415

acc ttc ggc gca ccc ggc caa gcc aac tac gcc gca gcc aac gcc tac   19350
Thr Phe Gly Ala Pro Gly Gln Ala Asn Tyr Ala Ala Ala Asn Ala Tyr
           6420                6425                6430

ctc gac gcc ctc gcc cac cac cgc cac acc cac cac ctc ccc gcc acc   19398
Leu Asp Ala Leu Ala His His Arg His Thr His His Leu Pro Ala Thr
       6435                6440                6445

agc atc gcc tgg ggc acc tgg caa gga aac gga ctg gcg act ggt caa   19446
Ser Ile Ala Trp Gly Thr Trp Gln Gly Asn Gly Leu Ala Thr Gly Gln
   6450                6455                6460

gtc agc gaa cat ctc cgc cgc cgc ggg atg ttc gcc atg ccg ccc gag   19494
Val Ser Glu His Leu Arg Arg Arg Gly Met Phe Ala Met Pro Pro Glu
6465                6470                6475                6480

ttg gcg gtc aca gct gtt gac ggc gcg atc gcg agc ggg cgc ccg agt   19542
Leu Ala Val Thr Ala Val Asp Gly Ala Ile Ala Ser Gly Arg Pro Ser
               6485                6490                6495

ctc ctc gtc gcc gat atc gac tgg aag aaa ttg gga ccg gtt ctc tcc   19590
Leu Leu Val Ala Asp Ile Asp Trp Lys Lys Leu Gly Pro Val Leu Ser
           6500                6505                6510

agc aag tcg tcg gtc ttg ctc gag gac ctt ccc cag gca cag gga act   19638
Ser Lys Ser Ser Val Leu Leu Glu Asp Leu Pro Gln Ala Gln Gly Thr
       6515                6520                6525

gag gag gcg cgc agt acc gtt gag cag acg gag agc aca aac ctc cgg   19686
Glu Glu Ala Arg Ser Thr Val Glu Gln Thr Glu Ser Thr Asn Leu Arg
   6530                6535                6540

caa ctc ctc atg ggt cgg tca cgt tcc gag cag gaa gaa gag ctg ctc   19734
Gln Leu Leu Met Gly Arg Ser Arg Ser Glu Gln Glu Glu Glu Leu Leu
6545                6550                6555                6560
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agc ctc gtc cgc atc cac tcc gcg gca gtg ctc ggg cgc gac gac tcc   19782
Ser Leu Val Arg Ile His Ser Ala Ala Val Leu Gly Arg Asp Asp Ser
               6565                6570                6575

gag gcc atc ccg ccc ggt cgg ctg ttc agg gat cta ggg ttc gac tcg   19830
Glu Ala Ile Pro Pro Gly Arg Leu Phe Arg Asp Leu Gly Phe Asp Ser
           6580                6585                6590

ctt gcg gcg gtg gag ctt cgc aac cac ctc gca gca cag acg gag ctg   19878
Leu Ala Ala Val Glu Leu Arg Asn His Leu Ala Ala Gln Thr Glu Leu
       6595                6600                6605

gct ctg ccg acg act ctc gtc ttc gat tac ccc agc ccc acc aag ctc   19926
Ala Leu Pro Thr Thr Leu Val Phe Asp Tyr Pro Ser Pro Thr Lys Leu
   6610                6615                6620

gcc caa ttt ctg ctc tcc gag atc gcg gag ttc cag ccc gac aac tca   19974
Ala Gln Phe Leu Leu Ser Glu Ile Ala Glu Phe Gln Pro Asp Asn Ser
6625                6630                6635                6640

act ccg ctt ccg cga ccc cgg gca gag ctc gat gag ccg atc gcc atc   20022
Thr Pro Leu Pro Arg Pro Arg Ala Glu Leu Asp Glu Pro Ile Ala Ile
               6645                6650                6655

gtt ggc atg gcc tgt cgc ttc ccc ggc gga gtg acc tcg gcg gac gac   20070
Val Gly Met Ala Cys Arg Phe Pro Gly Gly Val Thr Ser Ala Asp Asp
           6660                6665                6670

ttc tgg gat ctg atc tcc tcc gag cag gac gcg atc ggc gga ttc ccc   20118
Phe Trp Asp Leu Ile Ser Ser Glu Gln Asp Ala Ile Gly Gly Phe Pro
       6675                6680                6685

acc gac cgc ggc tgg gac ctg gac acg ctc tac gac ccc gac ccc gac   20166
Thr Asp Arg Gly Trp Asp Leu Asp Thr Leu Tyr Asp Pro Asp Pro Asp
   6690                6695                6700

cac ccc ggc acc tgc tac acc cga aac ggc gga ttc ctc tac gac gca   20214
His Pro Gly Thr Cys Tyr Thr Arg Asn Gly Gly Phe Leu Tyr Asp Ala
6705                6710                6715                6720

ggc cac ttc gac gcc gaa ttc ttc ggc atc agc ccc cgc gaa gcc ctc   20262
Gly His Phe Asp Ala Glu Phe Phe Gly Ile Ser Pro Arg Glu Ala Leu
               6725                6730                6735

gcc atg gac ccc cag caa cga ctc ctc ctc gaa acc gcc tgg gaa acc   20310
Ala Met Asp Pro Gln Gln Arg Leu Leu Leu Glu Thr Ala Trp Glu Thr
           6740                6745                6750

atc gaa cac gcc ggc atc aac ccc cac acc ctc cac ggc acc ccc acc   20358
Ile Glu His Ala Gly Ile Asn Pro His Thr Leu His Gly Thr Pro Thr
       6755                6760                6765

gga gtc ttc acc ggc acc aac gga cag gac cac gcg gca cac atc cgt   20406
Gly Val Phe Thr Gly Thr Asn Gly Gln Asp His Ala Ala His Ile Arg
   6770                6775                6780

cag gcc ccg agc ggt acc gag gga ttc gtc ctg acc ggg gca gcc acc   20454
Gln Ala Pro Ser Gly Thr Glu Gly Phe Val Leu Thr Gly Ala Ala Thr
6785                6790                6795                6800
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agc atc gcc tcc ggc cga atc tcc tac atc ctc ggg ttg gaa ggg cct 20502
Ser Ile Ala Ser Gly Arg Ile Ser Tyr Ile Leu Gly Leu Glu Gly Pro
6805 6810 6815

gcg gtc acc ctc gac aca gcg tgt tcc tcc tcg ctc gtc gcc ctg cac 20550
Ala Val Thr Leu Asp Thr Ala Cys Ser Ser Ser Leu Val Ala Leu His
6820 6825 6830

ctc gcc tgc cag tcc ctc agg tcc ggt gaa tgc acc atg gcc ttg gcc 20598
Leu Ala Cys Gln Ser Leu Arg Ser Gly Glu Cys Thr Met Ala Leu Ala
6835 6840 6845

ggc ggg gcc acg gtc atg acc acc ccg atc acc ttc acc gaa ttc gcc 20646
Gly Gly Ala Thr Val Met Thr Thr Pro Ile Thr Phe Thr Glu Phe Ala
6850 6855 6860

cgc caa cgc gga ctc gcc ccc gac ggg cgt tgc aag gcg ttc tcg gcg 20694
Arg Gln Arg Gly Leu Ala Pro Asp Gly Arg Cys Lys Ala Phe Ser Ala
6865 6870 6875 6880

gcg gct gac ggt acc ggc tgg ggt gag ggt gtg ggg atg ctg ctg gtg 20742
Ala Ala Asp Gly Thr Gly Trp Gly Glu Gly Val Gly Met Leu Leu Val
6885 6890 6895

gag cgg ctc tcc gac gcc cgc cgc aac ggt cac cgt gtc ctg gcc gtg 20790
Glu Arg Leu Ser Asp Ala Arg Arg Asn Gly His Arg Val Leu Ala Val
6900 6905 6910

gtg cgt ggc agt gcg gtc aac cag gac ggt gcg agc aac ggt ctg acc 20838
Val Arg Gly Ser Ala Val Asn Gln Asp Gly Ala Ser Asn Gly Leu Thr
6915 6920 6925

gcg ccc aac ggg ccc tcc cag cag cgc gtc atc cgc cag gcc ctc gcc 20886
Ala Pro Asn Gly Pro Ser Gln Gln Arg Val Ile Arg Gln Ala Leu Ala
6930 6935 6940

aac gcg gac ctg acc ccc gcc gac gtc gat gcg gtg gag gcc cac ggc 20934
Asn Ala Asp Leu Thr Pro Ala Asp Val Asp Ala Val Glu Ala His Gly
6945 6950 6955 6960

acc ggc acc act ttg ggc gac ccg atc gag gcc cag gcc atc ctc gcg 20982
Thr Gly Thr Thr Leu Gly Asp Pro Ile Glu Ala Gln Ala Ile Leu Ala
6965 6970 6975

acc tac gga cag gac cgt ccc ggc aac ggg ccg ttg tgg ctg ggc tcc 21030
Thr Tyr Gly Gln Asp Arg Pro Gly Asn Gly Pro Leu Trp Leu Gly Ser
6980 6985 6990

gtc aag tcc aac gtc gga cac aca cag gcc gcg gcg ggc gtg gcc gga 21078
Val Lys Ser Asn Val Gly His Thr Gln Ala Ala Ala Gly Val Ala Gly
6995 7000 7005

gtg atc aag atg gtg atg gcc ctc cgc cac cgg aca ctc cca ccg act 21126
Val Ile Lys Met Val Met Ala Leu Arg His Arg Thr Leu Pro Pro Thr
7010 7015 7020

ctc cac gcg gat gag ccg tcg ccg cat gtg gac tgg tcc gcg ggt gcg 21174
Leu His Ala Asp Glu Pro Ser Pro His Val Asp Trp Ser Ala Gly Ala
7025 7030 7035 7040

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gtg cag ctg ctg acg gag acg gtg ccc tgg ccc ggc ggg gag ggg cgg   21222
Val Gln Leu Leu Thr Glu Thr Val Pro Trp Pro Gly Gly Glu Gly Arg
                7045                7050                7055

ccg cgg cgg gca gga gtg tca tca ttc ggc gtc agc ggc acc aac gcc   21270
Pro Arg Arg Ala Gly Val Ser Ser Phe Gly Val Ser Gly Thr Asn Ala
            7060                7065                7070

cac gtc atc ctc gaa gaa gca ccc gcc gac gac gtt ccg ggg gga cca   21318
His Val Ile Leu Glu Glu Ala Pro Ala Asp Asp Val Pro Gly Gly Pro
        7075                7080                7085

ccc gcc gac gag gat gcc ggt agt ggc gag gag gct gct gcc ggc agt   21366
Pro Ala Asp Glu Asp Ala Gly Ser Gly Glu Glu Ala Ala Ala Gly Ser
    7090                7095                7100

cct ggg gtg tgg ccg tgg ctg gtg tcg gcc aag tcg cag ccg gcc ctg   21414
Pro Gly Val Trp Pro Trp Leu Val Ser Ala Lys Ser Gln Pro Ala Leu
7105                7110                7115                7120

cgc gcc cag gcc cag gcc ctg cac gcc cac ctc acc gac cac ccc ggc   21462
Arg Ala Gln Ala Gln Ala Leu His Ala His Leu Thr Asp His Pro Gly
                7125                7130                7135

ctc gac ctc gcc gac gtc gga tac acc ctc gcc cac gcc cgc gcc gtg   21510
Leu Asp Leu Ala Asp Val Gly Tyr Thr Leu Ala His Ala Arg Ala Val
            7140                7145                7150

ttc gac cac cgc gcc acc ctc atc gcc gcc gac cgc gac acc ttc ctg   21558
Phe Asp His Arg Ala Thr Leu Ile Ala Ala Asp Arg Asp Thr Phe Leu
        7155                7160                7165

caa gca ctc cag gca ctc gcc gca ggc gaa ccc cac ccc gcc gtc atc   21606
Gln Ala Leu Gln Ala Leu Ala Ala Gly Glu Pro His Pro Ala Val Ile
    7170                7175                7180

cac agc agc gcc cca ggc ggg acc ggg acc ggg gag gcc gca gga aag   21654
His Ser Ser Ala Pro Gly Gly Thr Gly Thr Gly Glu Ala Ala Gly Lys
7185                7190                7195                7200

acc gca ttc atc tgc tcc gga cag ggc acc caa cgc ccc ggc atg gcc   21702
Thr Ala Phe Ile Cys Ser Gly Gln Gly Thr Gln Arg Pro Gly Met Ala
                7205                7210                7215

cac ggc ctc tac cac acc cac ccc gtc ttc gcc gcc gca ctc aac gac   21750
His Gly Leu Tyr His Thr His Pro Val Phe Ala Ala Ala Leu Asn Asp
            7220                7225                7230

atc tgc acc cac ctc gac ccc cac ctc gac cac ccc ctc ctc ccc ctc   21798
Ile Cys Thr His Leu Asp Pro His Leu Asp His Pro Leu Leu Pro Leu
        7235                7240                7245

ctc acc caa aac gac aac gac aac gac aac gag gac gcg gcc gca ctg   21846
Leu Thr Gln Asn Asp Asn Asp Asn Asp Asn Glu Asp Ala Ala Ala Leu
    7250                7255                7260

ctc cag cag acc ccg tac gcc cag ccc gcc ctc ttc gcc ttc cag gtc   21894
Leu Gln Gln Thr Pro Tyr Ala Gln Pro Ala Leu Phe Ala Phe Gln Val
7265                7270                7275                7280
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gcc ctc cac cgc ctc ctc acc gac ggc tac cac atc acc ccc cac tac   21942
Ala Leu His Arg Leu Leu Thr Asp Gly Tyr His Ile Thr Pro His Tyr
               7285                7290                7295

tac gcc gga cac tcc ctc ggc gaa atc acc gcc gcc cac ctc gcc ggc   21990
Tyr Ala Gly His Ser Leu Gly Glu Ile Thr Ala Ala His Leu Ala Gly
           7300                7305                7310

atc ctc acc ctc acc gac gcc acc acc ctc atc acc caa cgc gcc acc   22038
Ile Leu Thr Leu Thr Asp Ala Thr Thr Leu Ile Thr Gln Arg Ala Thr
       7315                7320                7325

ctc atg caa acc atg ccc ccc ggc acc atg acc acc ctc cac acc acc   22086
Leu Met Gln Thr Met Pro Pro Gly Thr Met Thr Thr Leu His Thr Thr
   7330                7335                7340

cca cac cac atc acc cac cac ctc acc gcc cac gaa aac gac ctc gcc   22134
Pro His His Ile Thr His His Leu Thr Ala His Glu Asn Asp Leu Ala
7345                7350                7355                7360

atc gcc gcc atc aac acc ccc acc tcc ctc gtc atc agc ggc acc ccc   22182
Ile Ala Ala Ile Asn Thr Pro Thr Ser Leu Val Ile Ser Gly Thr Pro
               7365                7370                7375

cac acc gtc caa cac atc acc acc ctc tgc caa caa caa ggc atc aaa   22230
His Thr Val Gln His Ile Thr Thr Leu Cys Gln Gln Gln Gly Ile Lys
           7380                7385                7390

acc aaa acc ctc ccc acc aac cac gcc ttc cac tcc ccc cac acc aac   22278
Thr Lys Thr Leu Pro Thr Asn His Ala Phe His Ser Pro His Thr Asn
       7395                7400                7405

ccc atc ctc aac caa ctc cac cag cac acc caa acc ctc acc tac cac   22326
Pro Ile Leu Asn Gln Leu His Gln His Thr Gln Thr Leu Thr Tyr His
   7410                7415                7420

cca ccc cac acc ccc ctc atc acc gcc aac acc cca ccc gac caa ctc   22374
Pro Pro His Thr Pro Leu Ile Thr Ala Asn Thr Pro Pro Asp Gln Leu
7425                7430                7435                7440

ctc acc ccc cac tac tgg acc caa caa gcc cgc aac acc gtc gac tac   22422
Leu Thr Pro His Tyr Trp Thr Gln Gln Ala Arg Asn Thr Val Asp Tyr
               7445                7450                7455

gcc acc acc acc caa acc ctc cac caa cac ggc gtc acc acc tac atc   22470
Ala Thr Thr Thr Gln Thr Leu His Gln His Gly Val Thr Thr Tyr Ile
           7460                7465                7470

gaa ctc gga ccc gac aac acc ctc acc acc ctc acc cac cac aac ctc   22518
Glu Leu Gly Pro Asp Asn Thr Leu Thr Thr Leu Thr His His Asn Leu
       7475                7480                7485

ccc aac acc ccc acc acc acc ctc acc ctc acc cac ccc cac cac cac   22566
Pro Asn Thr Pro Thr Thr Thr Leu Thr Leu Thr His Pro His His His
   7490                7495                7500

ccc caa acc cac ctc ctc acc aac ctc gcc aaa acc acc acc acc tgg   22614
Pro Gln Thr His Leu Leu Thr Asn Leu Ala Lys Thr Thr Thr Thr Trp
7505                7510                7515                7520
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cac ccc cac cac tac acc cac cac cac aac caa ccc cac acc cac acc   22662
His Pro His His Tyr Thr His His His Asn Gln Pro His Thr His Thr
               7525                7530                7535

cac ctc gac ctc ccc acc tac ccc ttc caa cac cac cac tac tgg ctc   22710
His Leu Asp Leu Pro Thr Tyr Pro Phe Gln His His His Tyr Trp Leu
           7540                7545                7550

gaa cta ccc agc gcc caa acc agc ccc ggt caa agg cgt tct cgc cgc   22758
Glu Leu Pro Ser Ala Gln Thr Ser Pro Gly Gln Arg Arg Ser Arg Arg
       7555                7560                7565

tcg gct cca gac acc gcc gag tcg gag ttc tgg gac gcg gtg aac gag   22806
Ser Ala Pro Asp Thr Ala Glu Ser Glu Phe Trp Asp Ala Val Asn Glu
   7570                7575                7580

gaa gac ctc cag agc ctc gcc gaa acc ctc gac atc gac gcc tct gct   22854
Glu Asp Leu Gln Ser Leu Ala Glu Thr Leu Asp Ile Asp Ala Ser Ala
7585                7590                7595                7600

ctg gac acg gtg gtg ccc gca ctc tcc gcc tgg cac cgc cac caa cac   22902
Leu Asp Thr Val Val Pro Ala Leu Ser Ala Trp His Arg His Gln His
               7605                7610                7615

gac caa gcc cgc atc aac acc tgg acc tac cag gaa acc tgg aaa ccc   22950
Asp Gln Ala Arg Ile Asn Thr Trp Thr Tyr Gln Glu Thr Trp Lys Pro
           7620                7625                7630

ctc acc ctc ccc acc acc cac caa ccc cac caa acc tgg ctc atc gcc   22998
Leu Thr Leu Pro Thr Thr His Gln Pro His Gln Thr Trp Leu Ile Ala
       7635                7640                7645

atc ccc gaa acc cag acc cac cac ccc cac atc acc aac atc ctc acc   23046
Ile Pro Glu Thr Gln Thr His His Pro His Ile Thr Asn Ile Leu Thr
   7650                7655                7660

aac ctc cac cac cac ggc atc acc ccc atc ccc ctc act gtc aac cac   23094
Asn Leu His His His Gly Ile Thr Pro Ile Pro Leu Thr Val Asn His
7665                7670                7675                7680

acc cac acc aac ccc caa cac ctc cac cac acc ctc cac cac acc cga   23142
Thr His Thr Asn Pro Gln His Leu His His Thr Leu His His Thr Arg
               7685                7690                7695

caa caa gcc caa aac cac acc acc gga ccc atc acc ggc ctg ctc tcc   23190
Gln Gln Ala Gln Asn His Thr Thr Gly Pro Ile Thr Gly Leu Leu Ser
           7700                7705                7710

ctc ctc gcc ctc gac gaa aca ccc cac ccc cac cac ccc cac aca ccc   23238
Leu Leu Ala Leu Asp Glu Thr Pro His Pro His His Pro His Thr Pro
       7715                7720                7725

acc ggc acc ctc ctc aac ctc acc ctc ccc caa acc cac acc caa acc   23286
Thr Gly Thr Leu Leu Asn Leu Thr Leu Pro Gln Thr His Thr Gln Thr
   7730                7735                7740

cac cca cca acc ccc ctc tgg tac gcc acc acc aac gcc acc acc acc   23334
His Pro Pro Thr Pro Leu Trp Tyr Ala Thr Thr Asn Ala Thr Thr Thr
7745                7750                7755                7760
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cac ccc aac gac ccc ctc aca cac ccc acc caa gcc caa acc tgg gga   23382
His Pro Asn Asp Pro Leu Thr His Pro Thr Gln Ala Gln Thr Trp Gly
               7765                7770                7775

ctc gcc cgc acc acc ctc ctc gaa cac ccc acc cac acc gcc gga atc   23430
Leu Ala Arg Thr Thr Leu Leu Glu His Pro Thr His Thr Ala Gly Ile
           7780                7785                7790

atc gac ctc ccc acc acc ccc acc ccc cac acc ctc cac cac ctc acc   23478
Ile Asp Leu Pro Thr Thr Pro Thr Pro His Thr Leu His His Leu Thr
       7795                7800                7805

caa acc ctc acc caa ccc cac cac caa acc caa ctc gcc atc cgc acc   23526
Gln Thr Leu Thr Gln Pro His His Gln Thr Gln Leu Ala Ile Arg Thr
   7810                7815                7820

acc ggc acc cac acc cgc cgc ctc acc ccc acc acc ctc acc ccc aca   23574
Thr Gly Thr His Thr Arg Arg Leu Thr Pro Thr Thr Leu Thr Pro Thr
7825                7830                7835                7840

cac caa cca ccc acc ccc acc ccc cac gga acc acc ctc atc acc ggc   23622
His Gln Pro Pro Thr Pro Thr Pro His Gly Thr Thr Leu Ile Thr Gly
               7845                7850                7855

gga acc ggc gcc ctc gcc acc cac ctc acc cac cac ctc acc acc cac   23670
Gly Thr Gly Ala Leu Ala Thr His Leu Thr His His Leu Thr Thr His
           7860                7865                7870

caa ccc acc caa cac ctc ctc ctc acc agc cga acc ggc ccc cac acc   23718
Gln Pro Thr Gln His Leu Leu Leu Thr Ser Arg Thr Gly Pro His Thr
       7875                7880                7885

ccc cac gca caa cac ctc acc acc caa ctc caa caa aaa ggc atc cac   23766
Pro His Ala Gln His Leu Thr Thr Gln Leu Gln Gln Lys Gly Ile His
   7890                7895                7900

ctc acc atc acc acc tgc gac acc agc aac cca gac caa ctc caa caa   23814
Leu Thr Ile Thr Thr Cys Asp Thr Ser Asn Pro Asp Gln Leu Gln Gln
7905                7910                7915                7920

ctc ctc aac acc atc ccc cca caa cac ccc ctc acc acc gtc atc cac   23862
Leu Leu Asn Thr Ile Pro Pro Gln His Pro Leu Thr Thr Val Ile His
               7925                7930                7935

acc gca ggc gtc aat ctc ttc gcc ccc gtg tcg gaa acc gat gcc gaa   23910
Thr Ala Gly Val Asn Leu Phe Ala Pro Val Ser Glu Thr Asp Ala Glu
           7940                7945                7950

tcc ttc tct tcc gtt acg gca gcg aag gca acg ggc gcg gcg att ctg   23958
Ser Phe Ser Ser Val Thr Ala Ala Lys Ala Thr Gly Ala Ala Ile Leu
       7955                7960                7965

cat gag ttg ctg ctg gac cat gaa acg ctt gaa cac ttc att ctc ttc   24006
His Glu Leu Leu Leu Asp His Glu Thr Leu Glu His Phe Ile Leu Phe
   7970                7975                7980

tcg tcg ggc gcc ggc gct tgg ggc agc ggg aat cag tgc gca tac tcg   24054
Ser Ser Gly Ala Gly Ala Trp Gly Ser Gly Asn Gln Cys Ala Tyr Ser
7985                7990                7995                8000
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gcg gcc aac gca tac ctg gac gcg ctc gcg acg cat cgt cag aca cat   24102
Ala Ala Asn Ala Tyr Leu Asp Ala Leu Ala Thr His Arg Gln Thr His
               8005                8010                8015

gga ctt ccc ggg gca tcg atc gcc tgg ggc ccc tgg gcc gga aag ggc   24150
Gly Leu Pro Gly Ala Ser Ile Ala Trp Gly Pro Trp Ala Gly Lys Gly
           8020                8025                8030

atg tcg gcc ggt gat gcg gct cat ggt tac ctg gaa aag cgc ggc att   24198
Met Ser Ala Gly Asp Ala Ala His Gly Tyr Leu Glu Lys Arg Gly Ile
       8035                8040                8045

ctg ccg atg gag cca cgc atg gcg ctc gcg gca ttc cat cgt gcg cgg   24246
Leu Pro Met Glu Pro Arg Met Ala Leu Ala Ala Phe His Arg Ala Arg
   8050                8055                8060

gcg cag cgg ccg aat tcc aac ctg atc atc gcg gac atc gac tgg gag   24294
Ala Gln Arg Pro Asn Ser Asn Leu Ile Ile Ala Asp Ile Asp Trp Glu
8065                8070                8075                8080

cgc ttc gtc ccc gcc ttc acc gct cga cgc cac agc ccg ctc atc gag   24342
Arg Phe Val Pro Ala Phe Thr Ala Arg Arg His Ser Pro Leu Ile Glu
               8085                8090                8095

gac att ccg gag gtt cgg caa gcg gct cag gag ctg gaa gca gct gcg   24390
Asp Ile Pro Glu Val Arg Gln Ala Ala Gln Glu Leu Glu Ala Ala Ala
           8100                8105                8110

tcg acg gca aag acg acc aca gct cag ccg att gcg acg tct ctc cgt   24438
Ser Thr Ala Lys Thr Thr Thr Ala Gln Pro Ile Ala Thr Ser Leu Arg
       8115                8120                8125

gag cga ttg gcc cga ctg acg tcc tca aag cag aac cag gtg ctg ctc   24486
Glu Arg Leu Ala Arg Leu Thr Ser Ser Lys Gln Asn Gln Val Leu Leu
   8130                8135                8140

ggc ctg att cgg aca ggc atc tgc acc gtt ctc ggc ctt cgt aat ccg   24534
Gly Leu Ile Arg Thr Gly Ile Cys Thr Val Leu Gly Leu Arg Asn Pro
8145                8150                8155                8160

gaa ggc atc gag gac caa cga gcc ttc cgc gac ctc ggc ttc gac tcg   24582
Glu Gly Ile Glu Asp Gln Arg Ala Phe Arg Asp Leu Gly Phe Asp Ser
               8165                8170                8175

ctg acg tcg gct cag ttc agc aag gaa ctc gcc aag gaa acc gga ctg   24630
Leu Thr Ser Ala Gln Phe Ser Lys Glu Leu Ala Lys Glu Thr Gly Leu
           8180                8185                8190

cca ctc ccc ccg tcc ctg gtc ttc gac tat ccc acc ccg cag gaa tgt   24678
Pro Leu Pro Pro Ser Leu Val Phe Asp Tyr Pro Thr Pro Gln Glu Cys
       8195                8200                8205

gct gcc cat ctg cgc aca caa ctc gtc gac cta gac gac gaa gag gac   24726
Ala Ala His Leu Arg Thr Gln Leu Val Asp Leu Asp Asp Glu Glu Asp
   8210                8215                8220

gcg gca ctg tcg aat gct ctc ccg caa gtg gcc cat cgg cgt acc gtc   24774
Ala Ala Leu Ser Asn Ala Leu Pro Gln Val Ala His Arg Arg Thr Val
8225                8230                8235                8240
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gag gac gaa ccg atc gcc atc atc ggt atg gca tgt cgc ttc ccc ggc   24822
Glu Asp Glu Pro Ile Ala Ile Ile Gly Met Ala Cys Arg Phe Pro Gly
               8245                8250                8255

ggc gta cgt tct gcc gac gac ctg tgg gaa ttg ctc gct tcg ggt aag   24870
Gly Val Arg Ser Ala Asp Asp Leu Trp Glu Leu Leu Ala Ser Gly Lys
           8260                8265                8270

gac gct atc ggc gtc ttc ccg acc gac cgc ggc tgg gac ctg gac acg   24918
Asp Ala Ile Gly Val Phe Pro Thr Asp Arg Gly Trp Asp Leu Asp Thr
       8275                8280                8285

ctc tac gac ccc gac ccc gac cac ccc ggc acc tgc tac acc cga aac   24966
Leu Tyr Asp Pro Asp Pro Asp His Pro Gly Thr Cys Tyr Thr Arg Asn
   8290                8295                8300

ggc gga ttc ctc tac ggc gca ggc cac ttc gac gcc gaa ttc ttc ggc   25014
Gly Gly Phe Leu Tyr Gly Ala Gly His Phe Asp Ala Glu Phe Phe Gly
8305                8310                8315                8320

atc agc ccc cgc gaa gcc ctc gcc atg gac ccc cag caa cga ctc ctc   25062
Ile Ser Pro Arg Glu Ala Leu Ala Met Asp Pro Gln Gln Arg Leu Leu
               8325                8330                8335

ctc gaa acc gcc tgg gaa acc atc gaa cac gcc ggc atc aac ccc cac   25110
Leu Glu Thr Ala Trp Glu Thr Ile Glu His Ala Gly Ile Asn Pro His
           8340                8345                8350

acc ctc cac ggc acc ccc acc gga gtc ttc gcc gga atc aac gct caa   25158
Thr Leu His Gly Thr Pro Thr Gly Val Phe Ala Gly Ile Asn Ala Gln
       8355                8360                8365

gac cac gcc gcg cat atc cgc caa agc cgt gat gtg gag acc atc gag   25206
Asp His Ala Ala His Ile Arg Gln Ser Arg Asp Val Glu Thr Ile Glu
   8370                8375                8380

ggc tac gcc ctg acc ggc agt tcg gga agt gtg gcg tcc ggc cgg gtg   25254
Gly Tyr Ala Leu Thr Gly Ser Ser Gly Ser Val Ala Ser Gly Arg Val
8385                8390                8395                8400

gcc tac acg ctc ggg ctc gaa ggc ccc gcg gtg tcg gtg gat acg gcg   25302
Ala Tyr Thr Leu Gly Leu Glu Gly Pro Ala Val Ser Val Asp Thr Ala
               8405                8410                8415

tgt tcg tcg tcg ttg gtg gcg ttg cat tgg gcg gcg cag gcg ttg cgt   25350
Cys Ser Ser Ser Leu Val Ala Leu His Trp Ala Ala Gln Ala Leu Arg
           8420                8425                8430

gcg ggt gag tgt tcg atg gcg ctt gcc ggg ggt gtg acg gtg atg tcg   25398
Ala Gly Glu Cys Ser Met Ala Leu Ala Gly Gly Val Thr Val Met Ser
       8435                8440                8445

tct ccg ggt acg ttt gtg gag ttc tca cgt cag cgg ggt ctg gcc gcg   25446
Ser Pro Gly Thr Phe Val Glu Phe Ser Arg Gln Arg Gly Leu Ala Ala
   8450                8455                8460

gac ggg cgg tgc aag gcc tat tcg gcg gct gct gac ggt acc ggc tgg   25494
Asp Gly Arg Cys Lys Ala Tyr Ser Ala Ala Ala Asp Gly Thr Gly Trp
8465                8470                8475                8480
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gcc gag ggt gtg ggg atg ctg ctg gtg gag cgg ctc tcc gac gcc cgt   25542
Ala Glu Gly Val Gly Met Leu Leu Val Glu Arg Leu Ser Asp Ala Arg
                8485                8490                8495

cgc aac ggt cac cgt gtc ctg gcc gtg gtg cgt ggc agt gcg gtc aac   25590
Arg Asn Gly His Arg Val Leu Ala Val Val Arg Gly Ser Ala Val Asn
            8500                8505                8510

cag gac ggt gcg agc aac ggt ctg acc gcg ccc aac ggg ccc tcc cag   25638
Gln Asp Gly Ala Ser Asn Gly Leu Thr Ala Pro Asn Gly Pro Ser Gln
        8515                8520                8525

cag cgt gtc atc cgt cag gcc ctg gcc aat gcg gga ctg acc ccg gcc   25686
Gln Arg Val Ile Arg Gln Ala Leu Ala Asn Ala Gly Leu Thr Pro Ala
    8530                8535                8540

gat gtc gac gca gtg gag ggc cac ggc acc ggg acc act ctg ggg gac   25734
Asp Val Asp Ala Val Glu Gly His Gly Thr Gly Thr Thr Leu Gly Asp
8545                8550                8555                8560

ccg atc gag gcc cag gca ctc ctg gcc gcc tac gga caa cac cgc ccc   25782
Pro Ile Glu Ala Gln Ala Leu Leu Ala Ala Tyr Gly Gln His Arg Pro
                8565                8570                8575

cac cac cgc ccc ttg tgg ctg gga tcc ctc aaa tcc aac atc ggg cac   25830
His His Arg Pro Leu Trp Leu Gly Ser Leu Lys Ser Asn Ile Gly His
            8580                8585                8590

gca cag gcc gcc gcg ggc gtg ggc gga gtc atc aag atg gtg atg gcc   25878
Ala Gln Ala Ala Ala Gly Val Gly Gly Val Ile Lys Met Val Met Ala
        8595                8600                8605

ctg cgc aac ggg ctg ctg cca cag acc ctc cac gtg gac gag ccc acc   25926
Leu Arg Asn Gly Leu Leu Pro Gln Thr Leu His Val Asp Glu Pro Thr
    8610                8615                8620

ccc cag gtc gac tgg tcc aca ggc gca gta caa ctc ctg aca caa ccg   25974
Pro Gln Val Asp Trp Ser Thr Gly Ala Val Gln Leu Leu Thr Gln Pro
8625                8630                8635                8640

gtg ccc tgg ccc gcc gac ccg gcc ggc cgg cca cgc cac gcc ggc gtg   26022
Val Pro Trp Pro Ala Asp Pro Ala Gly Arg Pro Arg His Ala Gly Val
                8645                8650                8655

tca tca ttc ggc gtc agc ggc acc aac gcc cac atc atc ctc gaa gaa   26070
Ser Ser Phe Gly Val Ser Gly Thr Asn Ala His Ile Ile Leu Glu Glu
            8660                8665                8670

gca ccc act ccc cag gac agc gat acc gac gac gaa ccg cct gcc aac   26118
Ala Pro Thr Pro Gln Asp Ser Asp Thr Asp Asp Glu Pro Pro Ala Asn
        8675                8680                8685

gca cca gcc ctg ccc cat ccc ctc cct ctt ccc gtg ccg gtg tcg gcg   26166
Ala Pro Ala Leu Pro His Pro Leu Pro Leu Pro Val Pro Val Ser Ala
    8690                8695                8700

agg tct gag gcc ggg ttg cgg gcg cag gca cag gcg ttg cgc cag tac   26214
Arg Ser Glu Ala Gly Leu Arg Ala Gln Ala Gln Ala Leu Arg Gln Tyr
8705                8710                8715                8720
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gtg gca gcc cgc ccg gac atg tca cct gcc gac att ggt gcg ggt ctg   26262
Val Ala Ala Arg Pro Asp Met Ser Pro Ala Asp Ile Gly Ala Gly Leu
               8725                8730                8735

gcc cgc ggc cgg gcc gta ctg gaa cac cgc gcc gtc atc ctg gcc gcg   26310
Ala Arg Gly Arg Ala Val Leu Glu His Arg Ala Val Ile Leu Ala Ala
           8740                8745                8750

gac cgc gag gaa ctg gcg cag gca ctg aca gcc ctg gca gcc ggc gaa   26358
Asp Arg Glu Glu Leu Ala Gln Ala Leu Thr Ala Leu Ala Ala Gly Glu
       8755                8760                8765

ccc cac ccc cac atc acc aca ggc cac acc cgg ggc ggt gac cgc ggc   26406
Pro His Pro His Ile Thr Thr Gly His Thr Arg Gly Gly Asp Arg Gly
   8770                8775                8780

ggc gtc gtc ttc gtc ttc ccc gga cag ggc ggc cag tgg gcc ggg atg   26454
Gly Val Val Phe Val Phe Pro Gly Gln Gly Gly Gln Trp Ala Gly Met
8785                8790                8795                8800

ggc ctg acc ctg ctc acc tcc tca ccc gtg ttc gcc gaa cac atc gac   26502
Gly Leu Thr Leu Leu Thr Ser Ser Pro Val Phe Ala Glu His Ile Asp
               8805                8810                8815

gca tgc gag aaa gcc ctc acc ccc tgg gtg ccc tgg tcc ctg acc gac   26550
Ala Cys Glu Lys Ala Leu Thr Pro Trp Val Pro Trp Ser Leu Thr Asp
           8820                8825                8830

atc ctg cac cgc gac ccc gac gac ccc gca tgg caa caa gcc gac gtg   26598
Ile Leu His Arg Asp Pro Asp Asp Pro Ala Trp Gln Gln Ala Asp Val
       8835                8840                8845

gtc cag ccc gtg ctc ttc agc atc atg gtc tcc ctc gcc gcc ctg tgg   26646
Val Gln Pro Val Leu Phe Ser Ile Met Val Ser Leu Ala Ala Leu Trp
   8850                8855                8860

cgc tcc tac ggc atc gaa ccc gac gcg gtc ctc ggc cac tcc cag gga   26694
Arg Ser Tyr Gly Ile Glu Pro Asp Ala Val Leu Gly His Ser Gln Gly
8865                8870                8875                8880

gaa atc gcc gcc gcc cac atc tgc ggc gca ctc agc ctg aaa gac gcc   26742
Glu Ile Ala Ala Ala His Ile Cys Gly Ala Leu Ser Leu Lys Asp Ala
               8885                8890                8895

gcc aaa acc gtt gca ctg cgc agc cgc gca ctg gcc gcc gta cga ggc   26790
Ala Lys Thr Val Ala Leu Arg Ser Arg Ala Leu Ala Ala Val Arg Gly
           8900                8905                8910

cgg ggc gcc atg gcc tca ctg ccc ctg ccc gcc cag gac gtg cag cag   26838
Arg Gly Ala Met Ala Ser Leu Pro Leu Pro Ala Gln Asp Val Gln Gln
       8915                8920                8925

ctc att tcc gaa cgg tgg gaa ggg cag ttg tgg gtg gca gcc ctc aac   26886
Leu Ile Ser Glu Arg Trp Glu Gly Gln Leu Trp Val Ala Ala Leu Asn
   8930                8935                8940

ggc ccc cac tcc acc acc gtc tcc ggc gac acc aag gcg gtg gat gag   26934
Gly Pro His Ser Thr Thr Val Ser Gly Asp Thr Lys Ala Val Asp Glu
8945                8950                8955                8960
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gtg ctg gcg cac tgc acc gac acc ggc cta cgg gcc aaa cgc atc ccc   26982
Val Leu Ala His Cys Thr Asp Thr Gly Leu Arg Ala Lys Arg Ile Pro
               8965                8970                8975

gtc gac tac gcc tcc cac tgc ccc cac gtc caa ccc ctc cac gac gaa   27030
Val Asp Tyr Ala Ser His Cys Pro His Val Gln Pro Leu His Asp Glu
           8980                8985                8990

ctc ctg cac ctg ctg gga gac atc acc ccc cag ccg tcc acc gtg ccg   27078
Leu Leu His Leu Leu Gly Asp Ile Thr Pro Gln Pro Ser Thr Val Pro
       8995                9000                9005

ttc ttc tcc acc gtg gaa ggc acc tgg ctg gac acc aca acc ctg gac   27126
Phe Phe Ser Thr Val Glu Gly Thr Trp Leu Asp Thr Thr Thr Leu Asp
   9010                9015                9020

gcc gcc tac tgg tac cgc aac ctc cac cag ccc gtc cgc ttc agc cac   27174
Ala Ala Tyr Trp Tyr Arg Asn Leu His Gln Pro Val Arg Phe Ser His
9025                9030                9035                9040

gcc atc cag acc ctg acc gac gac gga cac cgc gcc ttc atc gaa atc   27222
Ala Ile Gln Thr Leu Thr Asp Asp Gly His Arg Ala Phe Ile Glu Ile
               9045                9050                9055

agc ccc cac ccc acc ctc gtc ccc gcc atc gaa gac acc acc gaa aac   27270
Ser Pro His Pro Thr Leu Val Pro Ala Ile Glu Asp Thr Thr Glu Asn
           9060                9065                9070

acc acc gaa aac atc acc gcg acc ggc agc ctc cgc cgc ggc gac aac   27318
Thr Thr Glu Asn Ile Thr Ala Thr Gly Ser Leu Arg Arg Gly Asp Asn
       9075                9080                9085

gac acc cac cgc ttc ctc acc gcc ctc gcc cac acc cac acc acc ggc   27366
Asp Thr His Arg Phe Leu Thr Ala Leu Ala His Thr His Thr Thr Gly
   9090                9095                9100

atc ggc aca ccc acc acc tgg cac cac cac tac acc caa acc cac ccc   27414
Ile Gly Thr Pro Thr Thr Trp His His His Tyr Thr Gln Thr His Pro
9105                9110                9115                9120

cac ccc aac ccc cac acc cac ctc gac ctg ccc acc tac ccc ttc caa   27462
His Pro Asn Pro His Thr His Leu Asp Leu Pro Thr Tyr Pro Phe Gln
               9125                9130                9135

cac cag cac tac tgg ctc caa cca ccc acc aca aca acc gac ctc acc   27510
His Gln His Tyr Trp Leu Gln Pro Pro Thr Thr Thr Thr Asp Leu Thr
           9140                9145                9150

acc acc ggc ctc acc ccc acc cac cac ccc ctc ctc acc gcc aca ctc   27558
Thr Thr Gly Leu Thr Pro Thr His His Pro Leu Leu Thr Ala Thr Leu
       9155                9160                9165

acc ctc gcc gac aac aac aca caa cta ctc acc ggc cgc ctc tcc cta   27606
Thr Leu Ala Asp Asn Asn Thr Gln Leu Leu Thr Gly Arg Leu Ser Leu
   9170                9175                9180

cgc acc cac ccc tgg ctc acc gac cac acc gtc gcc ggc atg gtc ctc   27654
Arg Thr His Pro Trp Leu Thr Asp His Thr Val Ala Gly Met Val Leu
9185                9190                9195                9200
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ctg ccg ggc acc gcg ctc ctc gaa ctc gcc ctc caa gcc ggc gaa cgg   27702
Leu Pro Gly Thr Ala Leu Leu Glu Leu Ala Leu Gln Ala Gly Glu Arg
              9205                9210                9215

gtg gac tgc cct cgg gtg gag gaa ctg acc ctg cac gca ccg ttg gtg   27750
Val Asp Cys Pro Arg Val Glu Glu Leu Thr Leu His Ala Pro Leu Val
          9220                9225                9230

atc ccg cac acc gag gac gtg acg ttg cag gtc acc gtt cgg gca gcc   27798
Ile Pro His Thr Glu Asp Val Thr Leu Gln Val Thr Val Arg Ala Ala
      9235                9240                9245

gat gag agt ggc cat cgc gcc ctc gcg atc cac tcg tac tcc ggc acc   27846
Asp Glu Ser Gly His Arg Ala Leu Ala Ile His Ser Tyr Ser Gly Thr
  9250                9255                9260

gcg tcg tcg gcg gac cgg gag tgg acc cgt cac gcc acg ggc ctc ctc   27894
Ala Ser Ser Ala Asp Arg Glu Trp Thr Arg His Ala Thr Gly Leu Leu
9265              9270                9275                9280

aca cac cac gcc gac acc gat cac cgt gcc gac acg cac acg gac gcg   27942
Thr His His Ala Asp Thr Asp His Arg Ala Asp Thr His Thr Asp Ala
              9285                9290                9295

tgc ctt ggc ggg agc tgg ccc ccg ccc ggc gcg cag ccc atc gaa ctg   27990
Cys Leu Gly Gly Ser Trp Pro Pro Pro Gly Ala Gln Pro Ile Glu Leu
          9300                9305                9310

ggc gac gtc tac ggt cgt atg gcg gcg gac tcg gac atc gcc tac ggg   28038
Gly Asp Val Tyr Gly Arg Met Ala Ala Asp Ser Asp Ile Ala Tyr Gly
      9315                9320                9325

ccg gtc ttc cag ggg ctg cac gcc gcc tgg agg ttc ggc gac gat gtc   28086
Pro Val Phe Gln Gly Leu His Ala Ala Trp Arg Phe Gly Asp Asp Val
  9330                9335                9340

ctg gcc gag gtg cgt ctg ccg gaa gag gct ctg cgc gat gct ccg gcg   28134
Leu Ala Glu Val Arg Leu Pro Glu Glu Ala Leu Arg Asp Ala Pro Ala
9345              9350                9355                9360

gcg gcc ttc ggt gtt cac ccg gcc ttg ctc gac gcg gcc ctg cac gcc   28182
Ala Ala Phe Gly Val His Pro Ala Leu Leu Asp Ala Ala Leu His Ala
              9365                9370                9375

acg gcg ctc acc ccc cag aac ggg gac ggc tcg acg gag aac gtc gcc   28230
Thr Ala Leu Thr Pro Gln Asn Gly Asp Gly Ser Thr Glu Asn Val Ala
          9380                9385                9390

cag gag agc atg cct gac cgc gca gcc cac cag gcg cga ctg ccg ttc   28278
Gln Glu Ser Met Pro Asp Arg Ala Ala His Gln Ala Arg Leu Pro Phe
      9395                9400                9405

agc tgg agc ggc gtg tcc ctg cac acg gcg ggc agt tcc gtg ttg cgc   28326
Ser Trp Ser Gly Val Ser Leu His Thr Ala Gly Ser Ser Val Leu Arg
  9410                9415                9420

gta cgg ctg tcg cgc agt ccg cag cac ggt aat gcc gtg gcc ctc acc   28374
Val Arg Leu Ser Arg Ser Pro Gln His Gly Asn Ala Val Ala Leu Thr
9425              9430                9435                9440
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gcg gcc gac gag gac ggt cgg ccg gtg gtg acg atc gag tcg ctc gcg   28422
Ala Ala Asp Glu Asp Gly Arg Pro Val Val Thr Ile Glu Ser Leu Ala
               9445                9450                9455

ctg cgg ccg gtg tcc acc gag gag ctg cgc gcg gcc gcg gat cgt acg   28470
Leu Arg Pro Val Ser Thr Glu Glu Leu Arg Ala Ala Ala Asp Arg Thr
           9460                9465                9470

ccc gag cac gag tcg ctc ttc cga ctg gac tgg gtt tcc gta cca gtg   28518
Pro Glu His Glu Ser Leu Phe Arg Leu Asp Trp Val Ser Val Pro Val
       9475                9480                9485

ccc gcc aac gcc cct tcg ccc acc gcg gac cgg ccc tgg gcg gtc atc   28566
Pro Ala Asn Ala Pro Ser Pro Thr Ala Asp Arg Pro Trp Ala Val Ile
   9490                9495                9500

ggc gcg ggc ctt ccc cac ctg ccc ggc ctg acg gag cac gag cac gtg   28614
Gly Ala Gly Leu Pro His Leu Pro Gly Leu Thr Glu His Glu His Val
9505                9510                9515                9520

acc gcg tat gac gag ccg gcg gac ctg ctt ctg gct ctg gac cgc ggt   28662
Thr Ala Tyr Asp Glu Pro Ala Asp Leu Leu Leu Ala Leu Asp Arg Gly
               9525                9530                9535

gct ccg ccg ccc ggt gtg ctg gtc gta ggt ggt gtc gcc cac acc gaa   28710
Ala Pro Pro Pro Gly Val Leu Val Val Gly Gly Val Ala His Thr Glu
           9540                9545                9550

gcc cgg gag tat tcc gcc gaa gcc ccc ggg gag cgc ggg acc gag gcc   28758
Ala Arg Glu Tyr Ser Ala Glu Ala Pro Gly Glu Arg Gly Thr Glu Ala
       9555                9560                9565

tgc gag gcc cgg ccg gac gtc gtg cac gtg ggc gtc gtg cac acg gct   28806
Cys Glu Ala Arg Pro Asp Val Val His Val Gly Val Val His Thr Ala
   9570                9575                9580

gcc gtg cac gcg gct gcc gcg cag atg ttg gcc agg ctc cag gcc tgg   28854
Ala Val His Ala Ala Ala Ala Gln Met Leu Ala Arg Leu Gln Ala Trp
9585                9590                9595                9600

ctg ggc gac gag cgc ctc gca gac agc cgg ctg ctc gtc ctg acg tgc   28902
Leu Gly Asp Glu Arg Leu Ala Asp Ser Arg Leu Leu Val Leu Thr Cys
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ggc gcg gtc gcc cgc gcc tcc ggc gac gat gcg acg gac ctg ccc ggg   28950
Gly Ala Val Ala Arg Ala Ser Gly Asp Asp Ala Thr Asp Leu Pro Gly
           9620                9625                9630

gcc gcc gtg tgg ggg ctg gtg cgt tcg gcg cag tcc gag cac ccg gac   28998
Ala Ala Val Trp Gly Leu Val Arg Ser Ala Gln Ser Glu His Pro Asp
       9635                9640                9645

cgc atc acg ctg ctg gac ttc gag cgg ggc aca gag gcg gag ccc ggt   29046
Arg Ile Thr Leu Leu Asp Phe Glu Arg Gly Thr Glu Ala Glu Pro Gly
   9650                9655                9660

cag ctg gcg acg gcg ctg aac tgc ggg gag cgg cag ctt gcc gtc cgc   29094
Gln Leu Ala Thr Ala Leu Asn Cys Gly Glu Arg Gln Leu Ala Val Arg
9665                9670                9675                9680
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aac gcc ggc ttg tcg gcc ggt gat gtc gat gcg gtg gag gcc cac ggc   21342
Asn Ala Gly Leu Ser Ala Gly Asp Val Asp Ala Val Glu Ala His Gly
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acc ggc acc act ttg ggc gac ccg atc gag gcc cag gcc ctc ctt gcg   21390
Thr Gly Thr Thr Leu Gly Asp Pro Ile Glu Ala Gln Ala Leu Leu Ala
7055               7060                7065                7070

acc tac ggg cag gac cgt gcc ggc gag ggg ccg ctg tgg ctg ggc tcg   21438
Thr Tyr Gly Gln Asp Arg Ala Gly Glu Gly Pro Leu Trp Leu Gly Ser
               7075                7080                7085

gtc aag tcc aat gtc ggt cac aca cag gct gcc gcg ggc gtc gcc ggg   21486
Val Lys Ser Asn Val Gly His Thr Gln Ala Ala Ala Gly Val Ala Gly
           7090                7095                7100

gtg atc aag atg gtg atg gcg ctg cgg aat ggt ctg ctg ccg cgg acg   21534
Val Ile Lys Met Val Met Ala Leu Arg Asn Gly Leu Leu Pro Arg Thr
       7105                7110                7115

ttg cat gtg gat gag ccg tcg ccg cat gtg gac tgg tcc gcg ggt gcg   21582
Leu His Val Asp Glu Pro Ser Pro His Val Asp Trp Ser Ala Gly Ala
   7120                7125                7130

gtg cag ctg ctg acg gag acg gtg ccc tgg ccc ggc ggg gag ggg cgg   21630
Val Gln Leu Leu Thr Glu Thr Val Pro Trp Pro Gly Gly Glu Gly Arg
7135               7140                7145                7150

cta cgg cgg gca gga gtg tca tca ttc ggc gtc agc ggc acc aac gcc   21678
Leu Arg Arg Ala Gly Val Ser Ser Phe Gly Val Ser Gly Thr Asn Ala
               7155                7160                7165

cac gtc atc ctc gaa gaa gca ccc gcc cac aac atc ccg tca gac aca   21726
His Val Ile Leu Glu Glu Ala Pro Ala His Asn Ile Pro Ser Asp Thr
           7170                7175                7180

ccc gcc gac gac gtt ccg ggg gga cca ccc gcc ggc gag gat gcc ggt   21774
Pro Ala Asp Asp Val Pro Gly Gly Pro Pro Ala Gly Glu Asp Ala Gly
       7185                7190                7195

agt ggc gag gag gct gct gcc ggc agt cca ggg gtg tgg ccg tgg ctg   21822
Ser Gly Glu Glu Ala Ala Ala Gly Ser Pro Gly Val Trp Pro Trp Leu
   7200                7205                7210

gtg tcg gcc aag tcg cag ccg gcc ctg cgc gcc cag gcc cag gcc ctg   21870
Val Ser Ala Lys Ser Gln Pro Ala Leu Arg Ala Gln Ala Gln Ala Leu
7215               7220                7225                7230

cac gcc cac ctc acc gac cac ccc ggc ctc gac ctc gcc gac gtc gga   21918
His Ala His Leu Thr Asp His Pro Gly Leu Asp Leu Ala Asp Val Gly
               7235                7240                7245

tac acc ctc gcc cac gcc cgc gcc gtg ttc gac cac cgc gcc acc ctc   21966
Tyr Thr Leu Ala His Ala Arg Ala Val Phe Asp His Arg Ala Thr Leu
           7250                7255                7260

atc gcc gcc gac cgc gac acc ttc ctg caa gca ctc cag gca ctc gcc   22014
Ile Ala Ala Asp Arg Asp Thr Phe Leu Gln Ala Leu Gln Ala Leu Ala
       7265                7270                7275
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ccc gga ggg ctg ttc acg cca cgg ctg gtg cgc gcg cca cgt gtc gcc   29142
Pro Gly Gly Leu Phe Thr Pro Arg Leu Val Arg Ala Pro Arg Val Ala
               9685                9690                9695

gac gcc gta ccc gcc gta ccc gcc gtg gcc gta ccg tca gcg ggt cac   29190
Asp Ala Val Pro Ala Val Pro Ala Val Ala Val Pro Ser Ala Gly His
           9700                9705                9710

gca gcc gta ccg gca gcg ggt ccc ttc ctt ccg ggc gga acg gtg ctg   29238
Ala Ala Val Pro Ala Ala Gly Pro Phe Leu Pro Gly Gly Thr Val Leu
       9715                9720                9725

atc acc ggc gga acc ggt gtc ctg ggc cgg ctc gtg gcc cgg cat ctg   29286
Ile Thr Gly Gly Thr Gly Val Leu Gly Arg Leu Val Ala Arg His Leu
   9730                9735                9740

gtg gag gcg cac ggc gta cgg cat ctg ttg ctg gcg ggt cgg cgc gga   29334
Val Glu Ala His Gly Val Arg His Leu Leu Leu Ala Gly Arg Arg Gly
9745                9750                9755                9760

ccg gac gcc gag ggt gcg ccg gag ttg cgg gcg gag ctc ggt ggg ctc   29382
Pro Asp Ala Glu Gly Ala Pro Glu Leu Arg Ala Glu Leu Gly Gly Leu
               9765                9770                9775

ggc gcg acg gtg gag gtc gtc gcc tgc gac gcg gcg gac cgg cag cag   29430
Gly Ala Thr Val Glu Val Val Ala Cys Asp Ala Ala Asp Arg Gln Gln
           9780                9785                9790

ctg gcc gac ctg ctg aca cgg atc ccc gac gat cgg ccg ctg acc ggt   29478
Leu Ala Asp Leu Leu Thr Arg Ile Pro Asp Asp Arg Pro Leu Thr Gly
       9795                9800                9805

gtc gtg cac agt gcg ggc atc ctg gac gac ggc gtg atc acg tcg ctg   29526
Val Val His Ser Ala Gly Ile Leu Asp Asp Gly Val Ile Thr Ser Leu
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tcg ccg gag cgg ctc ggg gcc gtc ctc cgg gcc aag gcg gac gct gcg   29574
Ser Pro Glu Arg Leu Gly Ala Val Leu Arg Ala Lys Ala Asp Ala Ala
9825                9830                9835                9840

ctg ctt ctc gac gag ctg acg cgc ggg gca gag ctg tcg gct ttc gtc   29622
Leu Leu Leu Asp Glu Leu Thr Arg Gly Ala Glu Leu Ser Ala Phe Val
               9845                9850                9855

atg ttc tcc tcc gcg tcg gcg gtg gtc ggc tcg ccc ggg cag ggc aac   29670
Met Phe Ser Ser Ala Ser Ala Val Val Gly Ser Pro Gly Gln Gly Asn
           9860                9865                9870

tac gcc gcc gcc aac gcc gtc ctc gac ttc ctt gct cat cgc cgc cgc   29718
Tyr Ala Ala Ala Asn Ala Val Leu Asp Phe Leu Ala His Arg Arg Arg
       9875                9880                9885

gcc gag ggg ctg ccc gcc gtc tct ctc gcc tgg ggc ctg tgg gaa gag   29766
Ala Glu Gly Leu Pro Ala Val Ser Leu Ala Trp Gly Leu Trp Glu Glu
   9890                9895                9900

ggc aca ggg atg acg ggc cac ctc gac gtc gac gac cat gcg cgg atc   29814
Gly Thr Gly Met Thr Gly His Leu Asp Val Asp Asp His Ala Arg Ile
9905                9910                9915                9920
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Ser Arg Ala Gly Met Arg Pro Leu Pro Thr Ala Glu Ala Leu Ala Leu
9925 9930 9935

ttc gac gcg gcc ttg gcc gac ggc gag ccg ttc ctg atg ccg gct cgg 29910
Phe Asp Ala Ala Leu Ala Asp Gly Glu Pro Phe Leu Met Pro Ala Arg
9940 9945 9950

ctc gac ctc acg gcc gta cgg tct ggt gcc gcg tcc gca ccg gtg ccg 29958
Leu Asp Leu Thr Ala Val Arg Ser Gly Ala Ala Ser Ala Pro Val Pro
9955 9960 9965

ccg ctg ctg caa ggt ctg ctt cag ctg cct cgg tcc cgc tcg gcc gcc 30006
Pro Leu Leu Gln Gly Leu Leu Gln Leu Pro Arg Ser Arg Ser Ala Ala
9970 9975 9980

gcg gcc ccc ggc cat ggg gcc ccg gcg gcg gac gag gcg gcg gcc tgg 30054
Ala Ala Pro Gly His Gly Ala Pro Ala Ala Asp Glu Ala Ala Ala Trp
9985 9990 9995 10000

cgt gag cgt ctg gcc cgg cag agt gcc ggt gag cgc agg cag gcg ctg 30102
Arg Glu Arg Leu Ala Arg Gln Ser Ala Gly Glu Arg Arg Gln Ala Leu
10005 10010 10015

ctg cgc ctg gtg cgg tcg cat gtc gcg gcg gtg ctc ggc cat agc ggt 30150
Leu Arg Leu Val Arg Ser His Val Ala Ala Val Leu Gly His Ser Gly
10020 10025 10030

gcc gac gga atc gac gca tcg cgg gcg ttc cgc gag ctg ggg ttc gac 30198
Ala Asp Gly Ile Asp Ala Ser Arg Ala Phe Arg Glu Leu Gly Phe Asp
10035 10040 10045

tcg ctc acg gcg gtc gag ctg cgc aac cgt ctc acg gcc gcg acg ggc 30246
Ser Leu Thr Ala Val Glu Leu Arg Asn Arg Leu Thr Ala Ala Thr Gly
10050 10055 10060

ctg cgg ctg cgg gcc acg ctg gcc ttc gat ttc ccg acc ccg gca gcg 30294
Leu Arg Leu Arg Ala Thr Leu Ala Phe Asp Phe Pro Thr Pro Ala Ala
10065 10070 10075 10080

ctg gcc gag cac ttg ggc gag cgt ctg ctt ccc gac cag gag gcc acg 30342
Leu Ala Glu His Leu Gly Glu Arg Leu Leu Pro Asp Gln Glu Ala Thr
10085 10090 10095

ggc gag caa gcc ggc gat cag ctc tcc ggc ggc agc gag gag gac gta 30390
Gly Glu Gln Ala Gly Asp Gln Leu Ser Gly Gly Ser Glu Glu Asp Val
10100 10105 10110

cgc agc ctc ctg acg tcc att ccg atc ggc agg ctg cgg gac gcg ggg 30438
Arg Ser Leu Leu Thr Ser Ile Pro Ile Gly Arg Leu Arg Asp Ala Gly
10115 10120 10125

ctc ctc ggg ccc ctg ctc acg ctc gcg gac acg ggc cgc ggc gcc tcg 30486
Leu Leu Gly Pro Leu Leu Thr Leu Ala Asp Thr Gly Arg Gly Ala Ser
10130 10135 10140

ggc gcc gcc gca ggt ccg gag gac gcg ccg ccc tcc ggc cag gac aca 30534
Gly Ala Ala Ala Gly Pro Glu Asp Ala Pro Pro Ser Gly Gln Asp Thr
10145 10150 10155 10160

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ccg gct ccc gtc tcg atc gac gag atg gac atc gac gac ctg atg gat   30582
Pro Ala Pro Val Ser Ile Asp Glu Met Asp Ile Asp Asp Leu Met Asp
             10165               10170               10175

ctg gcg cac ggg cat ggc acc gca ccc gcc cgt gag ccc gcc gac gca   30630
Leu Ala His Gly His Gly Thr Ala Pro Ala Arg Glu Pro Ala Asp Ala
         10180               10185               10190

gag gac tcg tcg tca tca cga aac cgg aca cac cac aca cac gaa ggt   30678
Glu Asp Ser Ser Ser Ser Arg Asn Arg Thr His His Thr His Glu Gly
     10195               10200               10205

gag aca gcg tga                                                  30690
Glu Thr Ala
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gat ctc ctc aat gtg cgg cgt cga ctt cag cag att gaa tcg ggc gag   96
Asp Leu Leu Asn Val Arg Arg Arg Leu Gln Gln Ile Glu Ser Gly Glu
             20                  25                  30

cag gag ccg att gca att gtg ggg atg gcg tgc cgt ttt ccg ggg ggt   144
Gln Glu Pro Ile Ala Ile Val Gly Met Ala Cys Arg Phe Pro Gly Gly
         35                  40                  45

gtg gag tcg gcg gag gat ttc tgg gag ttg att gcg tcg ggt cgg gat   192
Val Glu Ser Ala Glu Asp Phe Trp Glu Leu Ile Ala Ser Gly Arg Asp
     50                  55                  60

gcg gtg ggg gag ttt ccg gtc gac cgg ggt tgg gac gtg gag gct ttc   240
Ala Val Gly Glu Phe Pro Val Asp Arg Gly Trp Asp Val Glu Ala Phe
 65                  70                  75                  80

tat gat ccg gag ccg ggg cgg gcg ggt tcg tcg tat acg cgc cgg ggc   288
Tyr Asp Pro Glu Pro Gly Arg Ala Gly Ser Ser Tyr Thr Arg Arg Gly
                 85                  90                  95

ggt ttc ctg gag ggt gcg gcg gag ttc gat gcg ggg ttt ttc ggg atc   336
Gly Phe Leu Glu Gly Ala Ala Glu Phe Asp Ala Gly Phe Phe Gly Ile
            100                 105                 110
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agt ccg cgt gag gcg ttg gcg atg gat ccg cag cag cgg ttg atg ctg   384
Ser Pro Arg Glu Ala Leu Ala Met Asp Pro Gln Gln Arg Leu Met Leu
        115                 120                 125

gag gtg tcc tgg gag gcg ttg gag cgg gcg ggc atc gac ccc gcc acg   432
Glu Val Ser Trp Glu Ala Leu Glu Arg Ala Gly Ile Asp Pro Ala Thr
    130                 135                 140

ttg cgc ggc agc cgg acg ggc gtc ttc gcc ggc ctc atg tcc cag gac   480
Leu Arg Gly Ser Arg Thr Gly Val Phe Ala Gly Leu Met Ser Gln Asp
145                 150                 155                 160

tac gcg acc cgt ctg ctc tcg gtc ccc gac gac ctg gcc ggc tac ctg   528
Tyr Ala Thr Arg Leu Leu Ser Val Pro Asp Asp Leu Ala Gly Tyr Leu
                165                 170                 175

ggc aac ggc aac gcg gga agc atc ctg tcc gga cgc gtc gcc tac acc   576
Gly Asn Gly Asn Ala Gly Ser Ile Leu Ser Gly Arg Val Ala Tyr Thr
            180                 185                 190

ttc ggc ttc gag ggc ccc gcg gtg acg gtc gac acg gcg tgc tcg tcg   624
Phe Gly Phe Glu Gly Pro Ala Val Thr Val Asp Thr Ala Cys Ser Ser
        195                 200                 205

tcg ctg gtg gca ctg cac ctc gcc tgc cag tca ctg cgc acc ggt gag   672
Ser Leu Val Ala Leu His Leu Ala Cys Gln Ser Leu Arg Thr Gly Glu
    210                 215                 220

tcc tcc ttc gcc ctc gcc gga ggc gtg acg gtc atg tcc acc ccg ggc   720
Ser Ser Phe Ala Leu Ala Gly Gly Val Thr Val Met Ser Thr Pro Gly
225                 230                 235                 240

atg ttc gtg gag ttc tcg cgg cag cgg ggt ctg tcg ccg gac ggc cgg   768
Met Phe Val Glu Phe Ser Arg Gln Arg Gly Leu Ser Pro Asp Gly Arg
                245                 250                 255

tgc aag gcg tac gcg tcg gct gcc gac ggc acc ggc atg tcc gag ggc   816
Cys Lys Ala Tyr Ala Ser Ala Ala Asp Gly Thr Gly Met Ser Glu Gly
            260                 265                 270

gtg ggg att ttg ctg ctg gag cgg ctg tcc gag gct gaa cgt cgt ggt   864
Val Gly Ile Leu Leu Leu Glu Arg Leu Ser Glu Ala Glu Arg Arg Gly
        275                 280                 285

cat cgg gtt ttg gcg gtg gtg cgg ggg agt gcg gtg aat cag gac ggt   912
His Arg Val Leu Ala Val Val Arg Gly Ser Ala Val Asn Gln Asp Gly
    290                 295                 300

gcg tcg aat ggg ttg acg gcg ccg aat ggt ccg tcg cag cag cgg gtg   960
Ala Ser Asn Gly Leu Thr Ala Pro Asn Gly Pro Ser Gln Gln Arg Val
305                 310                 315                 320

att cgg cag gcg ttg gcg tgt gcg ggg ttg tct gtg gcg gat gtg gat   1008
Ile Arg Gln Ala Leu Ala Cys Ala Gly Leu Ser Val Ala Asp Val Asp
                325                 330                 335

gtg gtg gag ggg cac ggg acg ggc acg acg ctg ggt gat ccg atc gag   1056
Val Val Glu Gly His Gly Thr Gly Thr Thr Leu Gly Asp Pro Ile Glu
            340                 345                 350
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gcg cag gcg ttg ctc gcc acg tac ggg cag cgg gcc ggt gac acg ccg   1104
Ala Gln Ala Leu Leu Ala Thr Tyr Gly Gln Arg Ala Gly Asp Thr Pro
        355                 360                 365

gtg tgg ttg ggg tcg gtg aag tcg aac atc ggg cat gcg cag gct gct   1152
Val Trp Leu Gly Ser Val Lys Ser Asn Ile Gly His Ala Gln Ala Ala
    370                 375                 380

gcg ggt gtg gcg ggt gtg atc aag atg gtg atg gcg ttg cgg gcg ggg   1200
Ala Gly Val Ala Gly Val Ile Lys Met Val Met Ala Leu Arg Ala Gly
385                 390                 395                 400

gtg ttg ccg cgg acg ttg cat gtg gat gag ccg tcg tcg cag gtg gat   1248
Val Leu Pro Arg Thr Leu His Val Asp Glu Pro Ser Ser Gln Val Asp
                405                 410                 415

tgg tcg agt ggg tcg gtt cgt gtg ttg gcg gat gag gtg gag tgg ccg   1296
Trp Ser Ser Gly Ser Val Arg Val Leu Ala Asp Glu Val Glu Trp Pro
            420                 425                 430

ggg gtg gag ggt cgg ctg cgg cgt gcg ggg gtg tct gcg ttc ggg gtg   1344
Gly Val Glu Gly Arg Leu Arg Arg Ala Gly Val Ser Ala Phe Gly Val
        435                 440                 445

agt ggg acg aat gcg cat gtg att ttg gag gag gcg tcg ggg ggc gcg   1392
Ser Gly Thr Asn Ala His Val Ile Leu Glu Glu Ala Ser Gly Gly Ala
    450                 455                 460

ggt ggg ggt gcg ggc cgg ctg cag gag ttg ggt ccg ggg gtg gtg tcg   1440
Gly Gly Gly Ala Gly Arg Leu Gln Glu Leu Gly Pro Gly Val Val Ser
465                 470                 475                 480

ggt tcg ggg gtg gtg ccg tgg gtg gtg tcg gcg cgg tcg gag ttg gcg   1488
Gly Ser Gly Val Val Pro Trp Val Val Ser Ala Arg Ser Glu Leu Ala
                485                 490                 495

ttg cgg ggg cag gcg cgt cgg ttg cgt ggg gtt gtg gcg gtt ggt ggg   1536
Leu Arg Gly Gln Ala Arg Arg Leu Arg Gly Val Val Ala Val Gly Gly
            500                 505                 510

ggt gcg gat ggt gtg ggg gtg agt ccg gct ggg gtc ggg cgg gct ttg   1584
Gly Ala Asp Gly Val Gly Val Ser Pro Ala Gly Val Gly Arg Ala Leu
        515                 520                 525

gtg tcg gag cgg tcg gtg ttc gag cat cgt gcg gtg gtc gtg gcc gag   1632
Val Ser Glu Arg Ser Val Phe Glu His Arg Ala Val Val Val Ala Glu
    530                 535                 540

gac cgc gac gag ttc ctg cac gca ctc gac gca ctg gcc ggc ggc cgc   1680
Asp Arg Asp Glu Phe Leu His Ala Leu Asp Ala Leu Ala Gly Gly Arg
545                 550                 555                 560

ccc gtg ccc ggc gtc gtc gag gga cga acc acc tcg ggc gaa ctc gcc   1728
Pro Val Pro Gly Val Val Glu Gly Arg Thr Thr Ser Gly Glu Leu Ala
                565                 570                 575

gta ctc ttc gcc ggg cag gga acc cag cgc gca ggc atg ggc cgc gaa   1776
Val Leu Phe Ala Gly Gln Gly Thr Gln Arg Ala Gly Met Gly Arg Glu
            580                 585                 590
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ctg tac gag gcg tac ccc gtc ttc gcc cag gcc atc gac gag atc tgc   1824
Leu Tyr Glu Ala Tyr Pro Val Phe Ala Gln Ala Ile Asp Glu Ile Cys
        595                 600                 605

gcg gag gcc gac acc gcc cgc acc gac ccc ggt gcc cct ggg ctg cgg   1872
Ala Glu Ala Asp Thr Ala Arg Thr Asp Pro Gly Ala Pro Gly Leu Arg
    610                 615                 620

gac gta ctc ttc gca ccg cag gac tct ccc gaa ggc cgg ctg atc gag   1920
Asp Val Leu Phe Ala Pro Gln Asp Ser Pro Glu Gly Arg Leu Ile Glu
625                 630                 635                 640

gac acg ggt ttc gcc cag ccc gcc ctg ttc gcc ttc gag gtg gcg ctg   1968
Asp Thr Gly Phe Ala Gln Pro Ala Leu Phe Ala Phe Glu Val Ala Leu
                645                 650                 655

ttc cgg ctg ctg gag acc tgg ggt ctg acg ccc gac tac gtc ctc ggc   2016
Phe Arg Leu Leu Glu Thr Trp Gly Leu Thr Pro Asp Tyr Val Leu Gly
            660                 665                 670

cat tcc gtc ggt gaa ctg gcg gcc gcc cat gtc gcc ggg atg ctc tgc   2064
His Ser Val Gly Glu Leu Ala Ala Ala His Val Ala Gly Met Leu Cys
        675                 680                 685

ctt gcc gac gcg gtg gca ctg gtg gtc gca cga ggc cgc ctg atg caa   2112
Leu Ala Asp Ala Val Ala Leu Val Val Ala Arg Gly Arg Leu Met Gln
    690                 695                 700

ggg ctc ccg tcc ggc gga gcc atg gtg gcc atc gag gcg tcc gag gac   2160
Gly Leu Pro Ser Gly Gly Ala Met Val Ala Ile Glu Ala Ser Glu Asp
705                 710                 715                 720

gag atc ctc ccg ctg ccc gac gaa tac gca tcc cgg gtc gcg cac gcc   2208
Glu Ile Leu Pro Leu Pro Asp Glu Tyr Ala Ser Arg Val Ala His Ala
                725                 730                 735

gcg gtg aac ggg ccg cgg tcg atc gtc ctc tcc ggg gac gag gac gcg   2256
Ala Val Asn Gly Pro Arg Ser Ile Val Leu Ser Gly Asp Glu Asp Ala
            740                 745                 750

gtc ctg gac ctc gcg cag caa tgg gcg gca cga ggc cgc cgc acc cgg   2304
Val Leu Asp Leu Ala Gln Gln Trp Ala Ala Arg Gly Arg Arg Thr Arg
        755                 760                 765

cgg ctg cgg acc agc cac gcc ttc cac tcg ccg cac atg gac gcc atg   2352
Arg Leu Arg Thr Ser His Ala Phe His Ser Pro His Met Asp Ala Met
    770                 775                 780

ttg ggc gac ttc cgc cgc gcg gcc gag cag gtc acc ttc agc gcc ccg   2400
Leu Gly Asp Phe Arg Arg Ala Ala Glu Gln Val Thr Phe Ser Ala Pro
785                 790                 795                 800

cgg att ccc gtc gtc tcc aac gtc acc ggc gcg ccc ctc ccc gcc gag   2448
Arg Ile Pro Val Val Ser Asn Val Thr Gly Ala Pro Leu Pro Ala Glu
                805                 810                 815

acc atg tgc acc ccg gac tac tgg gtc gaa cac gcc cgc agc acg gtc   2496
Thr Met Cys Thr Pro Asp Tyr Trp Val Glu His Ala Arg Ser Thr Val
            820                 825                 830
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cgt ttc gcg gac ggc atc tca tgg ctt cag gaa cag ggc gtc acc acc   2544
Arg Phe Ala Asp Gly Ile Ser Trp Leu Gln Glu Gln Gly Val Thr Thr
        835                 840                 845

tgc ctc gaa atc ggc ccc gac ggc acg ctg tcg gcc ctc gca cag gac   2592
Cys Leu Glu Ile Gly Pro Asp Gly Thr Leu Ser Ala Leu Ala Gln Asp
    850                 855                 860

tcg ctc agt gca ccg gcc cgc gcc atc ccc gcc ctg cgg ccg gac cag   2640
Ser Leu Ser Ala Pro Ala Arg Ala Ile Pro Ala Leu Arg Pro Asp Gln
865                 870                 875                 880

ccg gag gca cgg tcg gtc atg acc gcc ctg gcg gag ttg ttc gtg gct   2688
Pro Glu Ala Arg Ser Val Met Thr Ala Leu Ala Glu Leu Phe Val Ala
                885                 890                 895

ggg acg gcg gtt gag tgg gcc ggt gtg ttc gag ggg act gct cgc gag   2736
Gly Thr Ala Val Glu Trp Ala Gly Val Phe Glu Gly Thr Ala Arg Glu
            900                 905                 910

gtc ggt gat gga tgc ggg gtg gag ctg ccg acg tat gcg ttt gag cgg   2784
Val Gly Asp Gly Cys Gly Val Glu Leu Pro Thr Tyr Ala Phe Glu Arg
        915                 920                 925

gag cga ttt tgg ctg gac gtg gag gag gga tct gcg gga ggt tcc ggg   2832
Glu Arg Phe Trp Leu Asp Val Glu Glu Gly Ser Ala Gly Gly Ser Gly
    930                 935                 940

gtt tcc ggg atg tgg ggt ggt ccg ttg tgg gag gcg gtc gag tgt ggt   2880
Val Ser Gly Met Trp Gly Gly Pro Leu Trp Glu Ala Val Glu Cys Gly
945                 950                 955                 960

gat gcg ggg gtg gtg gca tcg ctc ctt ggg gtg gat gag ggg gcg tcg   2928
Asp Ala Gly Val Val Ala Ser Leu Leu Gly Val Asp Glu Gly Ala Ser
                965                 970                 975

ctg ggt gcg gtg gtg tcg gcg ttg ggg gaa tgg ggg cgg gta cgg cac   2976
Leu Gly Ala Val Val Ser Ala Leu Gly Glu Trp Gly Arg Val Arg His
            980                 985                 990

gag cgt gaa gtg gtg gac ggg tgg cgc tat cgg gag gtg tgg cga ccc   3024
Glu Arg Glu Val Val Asp Gly Trp Arg Tyr Arg Glu Val Trp Arg Pro
        995                1000                1005

gtt tcg ggc ggt ggt gta ggg ggg ctg tcg ggc gcg tgg ctg gtg gtg   3072
Val Ser Gly Gly Gly Val Gly Gly Leu Ser Gly Ala Trp Leu Val Val
   1010                1015                1020

tcc gag ggc gag gcg ggc ccg gtt gat gtg gtg gcg gag ggg ttg gag   3120
Ser Glu Gly Glu Ala Gly Pro Val Asp Val Val Ala Glu Gly Leu Glu
1025                1030                1035                1040

cgg tgt ggg gcg cga gtg gtt cgg gtg gag gtg gaa gcg ggg tgt gtg   3168
Arg Cys Gly Ala Arg Val Val Arg Val Glu Val Glu Ala Gly Cys Val
                1045                1050                1055

agc agg gaa gtg ttg gcc ggc cac ctg cgt gag gcg gtc gat ggt gag   3216
Ser Arg Glu Val Leu Ala Gly His Leu Arg Glu Ala Val Asp Gly Glu
            1060                1065                1070
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gct gtc ggc ggt gtc gtc tcc ctt gtg ggc tgg ggg agt ggc gtc gtg   3264
Ala Val Gly Gly Val Val Ser Leu Val Gly Trp Gly Ser Gly Val Val
       1075                1080                1085

cag gcg gga gtg gcg tct gtg ggg ttg gtg cag gcg ctg ggt gat gtg   3312
Gln Ala Gly Val Ala Ser Val Gly Leu Val Gln Ala Leu Gly Asp Val
   1090                1095                1100

ggc gtg ggg gcg cgg ctg tgg tgt gtg acg ggc ggg gcc gtg tcg gtg   3360
Gly Val Gly Ala Arg Leu Trp Cys Val Thr Gly Gly Ala Val Ser Val
1105                1110                1115                1120

ggg ggc cgg gat gct gtg tgg ggg ccg gcc tcg ggt gtg gtg tgg ggg   3408
Gly Gly Arg Asp Ala Val Trp Gly Pro Ala Ser Gly Val Val Trp Gly
                1125                1130                1135

ctg ggc cgt gtg gtg ggg gcg gag gca ccg gac cgc tgg ggt ggg ctg   3456
Leu Gly Arg Val Val Gly Ala Glu Ala Pro Asp Arg Trp Gly Gly Leu
            1140                1145                1150

gtt gat gtg ccg gag ctc gtg gat gag cgg gtg gtc gat ggg ttg gta   3504
Val Asp Val Pro Glu Leu Val Asp Glu Arg Val Val Asp Gly Leu Val
       1155                1160                1165

ggt gtg ctg gcg ggt gtg ggg gga ggg ggt gag agt gag ttt gcc gtg   3552
Gly Val Leu Ala Gly Val Gly Gly Gly Gly Glu Ser Glu Phe Ala Val
   1170                1175                1180

cgg tct tcg ggg gcg ttt gtg cgg cgg ttg gtg cgg gcg ccg ttg gag   3600
Arg Ser Ser Gly Ala Phe Val Arg Arg Leu Val Arg Ala Pro Leu Glu
1185                1190                1195                1200

gag gcc gtc gcg gag cgg gag tgg cgg ccc cgc ggc acc gta ctc gtc   3648
Glu Ala Val Ala Glu Arg Glu Trp Arg Pro Arg Gly Thr Val Leu Val
                1205                1210                1215

acc gga ggc acc ggc gag ttg ggt gcg cac gtc gcc cgg tgg atg gcc   3696
Thr Gly Gly Thr Gly Glu Leu Gly Ala His Val Ala Arg Trp Met Ala
            1220                1225                1230

cgg cgt ggc gcc gaa cac ctg ctg ctg gtg agc cga cgc ggg gag agc   3744
Arg Arg Gly Ala Glu His Leu Leu Leu Val Ser Arg Arg Gly Glu Ser
       1235                1240                1245

gcc cag gga gtc gaa gaa ctc cga gcg gac ttg atg ggc ttg ggc gcg   3792
Ala Gln Gly Val Glu Glu Leu Arg Ala Asp Leu Met Gly Leu Gly Ala
   1250                1255                1260

cgg gtg tcg gtg gtg gcg tgt gat gcg gcg gac cgt gag gcg ttg gcg   3840
Arg Val Ser Val Val Ala Cys Asp Ala Ala Asp Arg Glu Ala Leu Ala
1265                1270                1275                1280

gag gtg ttg cgg tcg gcc gtt ccg gcg gag tgc ccg ctg ggt gtg gtg   3888
Glu Val Leu Arg Ser Ala Val Pro Ala Glu Cys Pro Leu Gly Val Val
                1285                1290                1295

gtg cat gcc gcg gga gtt gtg gat gac ggg gtg ttg gag ggg ttg tcg   3936
Val His Ala Ala Gly Val Val Asp Asp Gly Val Leu Glu Gly Leu Ser
            1300                1305                1310
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tcc gag cgt gtc acg ggg gtg ctg cgg gcg aag gcg ctg gcg gcc tgg   3984
Ser Glu Arg Val Thr Gly Val Leu Arg Ala Lys Ala Leu Ala Ala Trp
       1315                1320                1325

aat ctg cat gag ttg acg cgg ggg gcg gat ctt tcg ggg ttc gtg gtg   4032
Asn Leu His Glu Leu Thr Arg Gly Ala Asp Leu Ser Gly Phe Val Val
   1330                1335                1340

ttc tcg tcg gct gcg gcg acg ttc ggg ccg gcg gga cag ggg agt tac   4080
Phe Ser Ser Ala Ala Ala Thr Phe Gly Pro Ala Gly Gln Gly Ser Tyr
1345                1350                1355                1360

gcg gcg gcg aac gcg tat gtg gag gca atc gtt cgg cac cgg cgt ggt   4128
Ala Ala Ala Asn Ala Tyr Val Glu Ala Ile Val Arg His Arg Arg Gly
               1365                1370                1375

gag ggc ctg ccg ggg ttg gcg gtg gcg tgg ggt ccg tgg gct ggt ggg   4176
Glu Gly Leu Pro Gly Leu Ala Val Ala Trp Gly Pro Trp Ala Gly Gly
           1380                1385                1390

ggg atg gcg gag ggg gcc gtg ggg cag atg cgg cgt cgg ggt ctg gcg   4224
Gly Met Ala Glu Gly Ala Val Gly Gln Met Arg Arg Arg Gly Leu Ala
       1395                1400                1405

gcg atg acg ccg gag acg gcg ctg gtg gca ctg ggc cag gcg ttg gac   4272
Ala Met Thr Pro Glu Thr Ala Leu Val Ala Leu Gly Gln Ala Leu Asp
   1410                1415                1420

cat gac gag acc tgt gtg acg gtc gcc gac atc gac tgg gac cga ttc   4320
His Asp Glu Thr Cys Val Thr Val Ala Asp Ile Asp Trp Asp Arg Phe
1425                1430                1435                1440

acc gcc aac tcc ctc ccc ggc tcc cga ctc tcg ccc ctc atc agc gac   4368
Thr Ala Asn Ser Leu Pro Gly Ser Arg Leu Ser Pro Leu Ile Ser Asp
               1445                1450                1455

atc ccc gaa gca cgc ctc gcc cgg gaa acc acc gga ctc gac acc gcc   4416
Ile Pro Glu Ala Arg Leu Ala Arg Glu Thr Thr Gly Leu Asp Thr Ala
           1460                1465                1470

acc gca tcc ccc gac tcg ttc tcc gca cgg ctc aag gcc atg gac acc   4464
Thr Ala Ser Pro Asp Ser Phe Ser Ala Arg Leu Lys Ala Met Asp Thr
       1475                1480                1485

gcc gag cag gaa cgt gcg ctt ctc gac ctg gtc cgt acg tac gcg gcg   4512
Ala Glu Gln Glu Arg Ala Leu Leu Asp Leu Val Arg Thr Tyr Ala Ala
   1490                1495                1500

acc gtg ctc gga cac agc acc ccc acc gcc gta cgc cct gag cga gcc   4560
Thr Val Leu Gly His Ser Thr Pro Thr Ala Val Arg Pro Glu Arg Ala
1505                1510                1515                1520

ttc cgc gac ctg ggc ttc gtc tcc gtg agc gcc gtc gaa ctg cgc aac   4608
Phe Arg Asp Leu Gly Phe Val Ser Val Ser Ala Val Glu Leu Arg Asn
               1525                1530                1535

cgc ctc aac gcc gtc acc ggg ctc ctc ctg ccc acc acg ctg atc ttc   4656
Arg Leu Asn Ala Val Thr Gly Leu Leu Leu Pro Thr Thr Leu Ile Phe
           1540                1545                1550
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gac tac ccc act ccc tcc gcg ctg gcc gga tac ctc aag gaa cag ctg   4704
Asp Tyr Pro Thr Pro Ser Ala Leu Ala Gly Tyr Leu Lys Glu Gln Leu
       1555                1560                1565

gag gag ggc gcg ggc ggc cag cgt gac att gct cct ccg gtc ccg gcg   4752
Glu Glu Gly Ala Gly Gly Gln Arg Asp Ile Ala Pro Pro Val Pro Ala
   1570                1575                1580

tcg cgt gtc gac gtt gac gag ccg att gcg att gtg ggg atg gcg tgc   4800
Ser Arg Val Asp Val Asp Glu Pro Ile Ala Ile Val Gly Met Ala Cys
1585                1590                1595                1600

cgt ttt ccg ggg ggt gtg gag tcg gcg gag gac ttg tgg gaa ctg gtc   4848
Arg Phe Pro Gly Gly Val Glu Ser Ala Glu Asp Leu Trp Glu Leu Val
               1605                1610                1615

gcg tcg ggt cgg gat gcg gtg gga gag ttt ccg gtc gac cgg ggt tgg   4896
Ala Ser Gly Arg Asp Ala Val Gly Glu Phe Pro Val Asp Arg Gly Trp
           1620                1625                1630

gac gtg gag gct ttc tat gat ccg gag ccg ggg cgg gcg ggt tcg tcg   4944
Asp Val Glu Ala Phe Tyr Asp Pro Glu Pro Gly Arg Ala Gly Ser Ser
       1635                1640                1645

tat acg cgc cgg ggc ggt ttc ctg gag ggt gcg gcg gag ttc gat gcg   4992
Tyr Thr Arg Arg Gly Gly Phe Leu Glu Gly Ala Ala Glu Phe Asp Ala
   1650                1655                1660

ggg ttt ttc ggg atc agt ccg cgt gag gcg ttg gcg atg gat ccg cag   5040
Gly Phe Phe Gly Ile Ser Pro Arg Glu Ala Leu Ala Met Asp Pro Gln
1665                1670                1675                1680

cag cgg ttg atg ctg gag gtg tcc tgg gag gcg ttg gag cgg gcg ggc   5088
Gln Arg Leu Met Leu Glu Val Ser Trp Glu Ala Leu Glu Arg Ala Gly
               1685                1690                1695

atc gac ccc gcc acg ttg cgc ggg tcc acg acc ggt gtc ttc gcc ggc   5136
Ile Asp Pro Ala Thr Leu Arg Gly Ser Thr Thr Gly Val Phe Ala Gly
           1700                1705                1710

atg tgc agt cag gac tac gcc gac ctc gtg cgc cgg gcc acc gag gac   5184
Met Cys Ser Gln Asp Tyr Ala Asp Leu Val Arg Arg Ala Thr Glu Asp
       1715                1720                1725

ctc gag ggc tac gcc atg acg ggc ctg tcc agc agc gtc aca tcc gga   5232
Leu Glu Gly Tyr Ala Met Thr Gly Leu Ser Ser Ser Val Thr Ser Gly
   1730                1735                1740

cgc gtc gcc tac acc ctg ggg ctc gag ggt ccg gcg gtg acg gtg gat   5280
Arg Val Ala Tyr Thr Leu Gly Leu Glu Gly Pro Ala Val Thr Val Asp
1745                1750                1755                1760

acg gcg tgt tcg tcg tcg ttg gtg gcg ctg cat ctg gcg tgt cag gcg   5328
Thr Ala Cys Ser Ser Ser Leu Val Ala Leu His Leu Ala Cys Gln Ala
               1765                1770                1775

ttg agg tcg ggg gag tgt tcg ctg gcg ttg gcg ggg ggt gtg acg gtg   5376
Leu Arg Ser Gly Glu Cys Ser Leu Ala Leu Ala Gly Gly Val Thr Val
           1780                1785                1790
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atg tcg acg ccg ggt gcg ttt gtg gag ttc tcg cgg cag cgg ggt ctg   5424
Met Ser Thr Pro Gly Ala Phe Val Glu Phe Ser Arg Gln Arg Gly Leu
       1795                1800                1805

tcg ccg gac ggc cgg tgc aag gcg tac ggg tcg ggg gcc gat ggg gtc   5472
Ser Pro Asp Gly Arg Cys Lys Ala Tyr Gly Ser Gly Ala Asp Gly Val
   1810                1815                1820

ggc tgg gcc gag ggt gtg ggt gtg ctg ttg gtg gag cgg ctg tcc gag   5520
Gly Trp Ala Glu Gly Val Gly Val Leu Leu Val Glu Arg Leu Ser Glu
1825                1830                1835                1840

gct gaa cgt cgt ggt cat cgg gtt ttg gcg gtg gtg cgg ggg agt gcg   5568
Ala Glu Arg Arg Gly His Arg Val Leu Ala Val Val Arg Gly Ser Ala
               1845                1850                1855

gtg aat cag gac ggt gcg tcg aat ggg ttg acg gcg ccg aat ggt ccg   5616
Val Asn Gln Asp Gly Ala Ser Asn Gly Leu Thr Ala Pro Asn Gly Pro
           1860                1865                1870

tcg cag cag cgg gtg att cgg cag gcg ttg gcg tgt gcg ggg ttg tcc   5664
Ser Gln Gln Arg Val Ile Arg Gln Ala Leu Ala Cys Ala Gly Leu Ser
       1875                1880                1885

gtg gcg gat gtg gat gtg gtg gag ggg cac ggg acg ggt acg acg ttg   5712
Val Ala Asp Val Asp Val Val Glu Gly His Gly Thr Gly Thr Thr Leu
   1890                1895                1900

ggt gat ccg atc gag gcg cag gcg ttg ctc gcc act tat ggg cag ggt   5760
Gly Asp Pro Ile Glu Ala Gln Ala Leu Leu Ala Thr Tyr Gly Gln Gly
1905                1910                1915                1920

cgt tcg ggg gag cgg ccg gtg tgg ttg ggg tcg gtg aag tcg aac atc   5808
Arg Ser Gly Glu Arg Pro Val Trp Leu Gly Ser Val Lys Ser Asn Ile
               1925                1930                1935

ggg cat gcg cag gct gct gcg ggt gtg gcg ggt gtg atc aag atg gtg   5856
Gly His Ala Gln Ala Ala Ala Gly Val Ala Gly Val Ile Lys Met Val
           1940                1945                1950

atg gcg ttg cgg gcg ggg gtg ttg ccg cgg acg ttg cat gtg gat gag   5904
Met Ala Leu Arg Ala Gly Val Leu Pro Arg Thr Leu His Val Asp Glu
       1955                1960                1965

ccg tcg tcg cag gtg gat tgg tcg agt ggg tcg gtt cgt gtg ttg gcg   5952
Pro Ser Ser Gln Val Asp Trp Ser Ser Gly Ser Val Arg Val Leu Ala
   1970                1975                1980

gat gag gtg gag tgg ccg ggg gtg gag ggt cgg ctg cgg cgt gcg ggg   6000
Asp Glu Val Glu Trp Pro Gly Val Glu Gly Arg Leu Arg Arg Ala Gly
1985                1990                1995                2000

gtg tct gcg ttc ggg gtg agt ggg acg aat gcg cat gtg att ttg gag   6048
Val Ser Ala Phe Gly Val Ser Gly Thr Asn Ala His Val Ile Leu Glu
               2005                2010                2015

gag gcg tcc ggg ggc gcg gat ggg ggt gcg ggc cgg ctg cag gag ttg   6096
Glu Ala Ser Gly Gly Ala Asp Gly Gly Ala Gly Arg Leu Gln Glu Leu
           2020                2025                2030
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ggt ccg ggg gtg gtg tcg ggt tcg ggg gtg gtg ccg tgg gtg gtg tcg   6144
Gly Pro Gly Val Val Ser Gly Ser Gly Val Val Pro Trp Val Val Ser
       2035                2040                2045

gcg cgg tcg gag ttg gcg ttg cgg ggg cag gcg cgt cgg ttg cgt ggg   6192
Ala Arg Ser Glu Leu Ala Leu Arg Gly Gln Ala Arg Arg Leu Arg Gly
   2050                2055                2060

gtt gtg gcg gtt ggt ggg ggt gcg gat ggt gtg ggg gtg agt ccg gct   6240
Val Val Ala Val Gly Gly Gly Ala Asp Gly Val Gly Val Ser Pro Ala
2065                2070                2075                2080

ggg gtc ggg cgg gct ttg gtg tcg gag cgg tcg gtg ttc gag cat cgt   6288
Gly Val Gly Arg Ala Leu Val Ser Glu Arg Ser Val Phe Glu His Arg
                2085                2090                2095

gcg gtg gtc gtg gcc gag gac cgc gac gag ttc ctg cac gca ctc gac   6336
Ala Val Val Val Ala Glu Asp Arg Asp Glu Phe Leu His Ala Leu Asp
           2100                2105                2110

gca ctg gcc gag ggg gca ccc acc gcg ggg gtg gta cag ggt gtg gcc   6384
Ala Leu Ala Glu Gly Ala Pro Thr Ala Gly Val Val Gln Gly Val Ala
       2115                2120                2125

gga ccg gcg gcc gac gga aag atc gcc atg ctg ttc gga gga cag ggc   6432
Gly Pro Ala Ala Asp Gly Lys Ile Ala Met Leu Phe Gly Gly Gln Gly
   2130                2135                2140

acc cac tgg gaa ggc atg gcg cag gaa ctc ctc ggc tcc tca ccg gtc   6480
Thr His Trp Glu Gly Met Ala Gln Glu Leu Leu Gly Ser Ser Pro Val
2145                2150                2155                2160

ttc gcc cag cag atg tcc gac tgc gcc caa gcc ctc gaa ccg tac ctg   6528
Phe Ala Gln Gln Met Ser Asp Cys Ala Gln Ala Leu Glu Pro Tyr Leu
                2165                2170                2175

gac tgg tct ctc ctc gac gtc ctg cgc ggc gca ccg gac gca ccc cct   6576
Asp Trp Ser Leu Leu Asp Val Leu Arg Gly Ala Pro Asp Ala Pro Pro
           2180                2185                2190

ctg caa cgc gtc gat gtc gtc cag ccc gtc ctc ttc gcg gtg atg gtc   6624
Leu Gln Arg Val Asp Val Val Gln Pro Val Leu Phe Ala Val Met Val
       2195                2200                2205

tcg ctg gcg gcg ctc tgg cgc tcg tac ggt gta cac ccg gac gcg gtg   6672
Ser Leu Ala Ala Leu Trp Arg Ser Tyr Gly Val His Pro Asp Ala Val
   2210                2215                2220

gcc ggg cac tcg cag ggc gag atc gca gcg gcc tac gtc gcc ggt gca   6720
Ala Gly His Ser Gln Gly Glu Ile Ala Ala Ala Tyr Val Ala Gly Ala
2225                2230                2235                2240

ctc tcc ctc gac gac gcc gcc cgg gtc acc gcc ctg cgc agc cag gcg   6768
Leu Ser Leu Asp Asp Ala Ala Arg Val Thr Ala Leu Arg Ser Gln Ala
                2245                2250                2255

ctg gcc gca ctg gcc ggg cag ggg gcg atg gca tcg gtc ggt ctg ccg   6816
Leu Ala Ala Leu Ala Gly Gln Gly Ala Met Ala Ser Val Gly Leu Pro
           2260                2265                2270
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gtc gag aag ctg gag ccg cgt ctt gcg aca tgg ggc gac cgt ctg gtc   6864
Val Glu Lys Leu Glu Pro Arg Leu Ala Thr Trp Gly Asp Arg Leu Val
       2275                2280                2285

atc gcc gcc gtg aac ggg gcg cgt tcg gcc gtg gtc tcc ggg gag ccg   6912
Ile Ala Ala Val Asn Gly Ala Arg Ser Ala Val Val Ser Gly Glu Pro
   2290                2295                2300

gaa gcg gtc gac gcc ctg gtg gag gag ctg tca cac gaa gac gta ccg   6960
Glu Ala Val Asp Ala Leu Val Glu Glu Leu Ser His Glu Asp Val Pro
2305                2310                2315                2320

gcc cgc agg ctc atg gtc gac tgg gcg tcg cac tcc ccg cag gtc gag   7008
Ala Arg Arg Leu Met Val Asp Trp Ala Ser His Ser Pro Gln Val Glu
               2325                2330                2335

gcg atc cag ggg cgg ctg ctc gaa ctc ctc gcc ccc atc cgc gcg agg   7056
Ala Ile Gln Gly Arg Leu Leu Glu Leu Leu Ala Pro Ile Arg Ala Arg
           2340                2345                2350

acc ggc gac gtg ccc ttc tac tcc acc gtc acc ggc gaa cgc atc gac   7104
Thr Gly Asp Val Pro Phe Tyr Ser Thr Val Thr Gly Glu Arg Ile Asp
       2355                2360                2365

ggc acc gaa ctc gac gcc gac tac tgg tac cgc aac ctg cgc cag gtc   7152
Gly Thr Glu Leu Asp Ala Asp Tyr Trp Tyr Arg Asn Leu Arg Gln Val
   2370                2375                2380

gtc cgc ttc cgg gac gcg aca cag gcg ctg gtc cgc gcc ggc cac acc   7200
Val Arg Phe Arg Asp Ala Thr Gln Ala Leu Val Arg Ala Gly His Thr
2385                2390                2395                2400

gtc ttc atc gag gcg tgc ccg cat ccg gcc gtc gcg gtc ggt gtg cag   7248
Val Phe Ile Glu Ala Cys Pro His Pro Ala Val Ala Val Gly Val Gln
               2405                2410                2415

gaa acc ctg gac gag atg ggt gac ttg gac agc ctg gtc gtc gga tct   7296
Glu Thr Leu Asp Glu Met Gly Asp Leu Asp Ser Leu Val Val Gly Ser
           2420                2425                2430

ctg cgc cgg ggc gaa ggc ggc ttg cga cgc ttc ctg atg tcc gtg gcc   7344
Leu Arg Arg Gly Glu Gly Gly Leu Arg Arg Phe Leu Met Ser Val Ala
       2435                2440                2445

gag ttg ttc gtg ggt ggg gtg gcg gtt gag tgg tcc ggt gtg ttc ggg   7392
Glu Leu Phe Val Gly Gly Val Ala Val Glu Trp Ser Gly Val Phe Gly
   2450                2455                2460

agt gtt ggt cgc ggg gtc gct ggt ggt tgc ggg gtg gag ctg ccg acg   7440
Ser Val Gly Arg Gly Val Ala Gly Gly Cys Gly Val Glu Leu Pro Thr
2465                2470                2475                2480

tat gcg ttc gag cga gag cgc ttt tgg ctg gat gtg gag ggg gcg ccg   7488
Tyr Ala Phe Glu Arg Glu Arg Phe Trp Leu Asp Val Glu Gly Ala Pro
               2485                2490                2495

cgg ggt tcc ggg gtc tct ggg cag tgg ggt ggt cag ttg tcg gag gcg   7536
Arg Gly Ser Gly Val Ser Gly Gln Trp Gly Gly Gln Leu Ser Glu Ala
           2500                2505                2510
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gtg gac acc gtg cgc ggc ggc atg ctg cgc gac tgc ctc gcc gga ctc   7584
Val Asp Thr Val Arg Gly Gly Met Leu Arg Asp Cys Leu Ala Gly Leu
       2515                2520                2525

gac ccc gcc gca cag gcc gag acc gtg ctg gac ctg gtc ctt acc cat   7632
Asp Pro Ala Ala Gln Ala Glu Thr Val Leu Asp Leu Val Leu Thr His
   2530                2535                2540

gcc gcg gcc gtc ctt gga cac ggc acc gcc gat gcg gtg gtg ccc gag   7680
Ala Ala Ala Val Leu Gly His Gly Thr Ala Asp Ala Val Val Pro Glu
2545                2550                2555                2560

cgc gcc ttc cgc gac ctc ggt ttc gac tcc ctc acc gcc gtc gaa cta   7728
Arg Ala Phe Arg Asp Leu Gly Phe Asp Ser Leu Thr Ala Val Glu Leu
               2565                2570                2575

cgc aac cgc ctc aac acc gcc acg ggc ctg cgc ttc ccg agg acc ctg   7776
Arg Asn Arg Leu Asn Thr Ala Thr Gly Leu Arg Phe Pro Arg Thr Leu
           2580                2585                2590

gtg ttc gac cat ccc cgc ccg gtg gca ctc gcg gca cac atc cac gag   7824
Val Phe Asp His Pro Arg Pro Val Ala Leu Ala Ala His Ile His Glu
       2595                2600                2605

cag ctg agc ggc gga agc ccg acc acc ggc act gcc ctt gcc ctt gcc   7872
Gln Leu Ser Gly Gly Ser Pro Thr Thr Gly Thr Ala Leu Ala Leu Ala
   2610                2615                2620

ctt cgg gcc ccg gca ccg cgt gtg gat gtc gac gag ccg att gcc att   7920
Leu Arg Ala Pro Ala Pro Arg Val Asp Val Asp Glu Pro Ile Ala Ile
2625                2630                2635                2640

gtg ggg atg gcg tgc cgt ttt ccg ggg ggt gtg gag tcg gcg gag gat   7968
Val Gly Met Ala Cys Arg Phe Pro Gly Gly Val Glu Ser Ala Glu Asp
               2645                2650                2655

ttc tgg gag ttg atc gcg tcg ggt cgg gat gcg gtg ggg gag ttt ccg   8016
Phe Trp Glu Leu Ile Ala Ser Gly Arg Asp Ala Val Gly Glu Phe Pro
           2660                2665                2670

gtc gac cgg ggt tgg gac gtg gag gct ttc tat gat ccg gag ccg ggg   8064
Val Asp Arg Gly Trp Asp Val Glu Ala Phe Tyr Asp Pro Glu Pro Gly
       2675                2680                2685

cgg gcg ggt acg tcc tac acg cgg tgt ggt ggg ttt ttg cag ggt gcg   8112
Arg Ala Gly Thr Ser Tyr Thr Arg Cys Gly Gly Phe Leu Gln Gly Ala
   2690                2695                2700

gcg gag ttc gat gcg ggg ttt ttc ggg atc agt ccg cgt gag gcg ttg   8160
Ala Glu Phe Asp Ala Gly Phe Phe Gly Ile Ser Pro Arg Glu Ala Leu
2705                2710                2715                2720

gcg atg gat ccg cag cag cgg ttg atg ctg gag gtg tcc tgg gag gcg   8208
Ala Met Asp Pro Gln Gln Arg Leu Met Leu Glu Val Ser Trp Glu Ala
               2725                2730                2735

ttg gag cgg gcg ggc atc gac ccc gcc acg ctg cac ggg tcc acg acc   8256
Leu Glu Arg Ala Gly Ile Asp Pro Ala Thr Leu His Gly Ser Thr Thr
           2740                2745                2750
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ggt gtc ttc gcc ggc gtc tcg cag cag gac tac gcc gag ctc ctg cgc   8304
Gly Val Phe Ala Gly Val Ser Gln Gln Asp Tyr Ala Glu Leu Leu Arg
       2755                2760                2765

cgc ggc acc cag gac cac gag ggg tac gcg ctc acc ggc gtc tcc aac   8352
Arg Gly Thr Gln Asp His Glu Gly Tyr Ala Leu Thr Gly Val Ser Asn
   2770                2775                2780

agc gtc gtc tcc ggg cgg ctt tcc tac acc ttc ggc ttc gag ggt ccg   8400
Ser Val Val Ser Gly Arg Leu Ser Tyr Thr Phe Gly Phe Glu Gly Pro
2785                2790                2795                2800

gcg gtg acg gtg gat acg gcg tgt tcg tcg tcg ttg gtg gcg ctg cat   8448
Ala Val Thr Val Asp Thr Ala Cys Ser Ser Ser Leu Val Ala Leu His
               2805                2810                2815

ctg gcg tgt cag gcg ttg agg tcg ggg gag tgt tcg ctg gcg ttg gcg   8496
Leu Ala Cys Gln Ala Leu Arg Ser Gly Glu Cys Ser Leu Ala Leu Ala
           2820                2825                2830

ggg ggt gtg acg gtg atg tcg acg ccg ggt gcg ttt gtg gag ttc tcg   8544
Gly Gly Val Thr Val Met Ser Thr Pro Gly Ala Phe Val Glu Phe Ser
       2835                2840                2845

cgg cag cgg ggt ctg tcg ccg gac ggc cgg tgc aag gcg tac ggg tcg   8592
Arg Gln Arg Gly Leu Ser Pro Asp Gly Arg Cys Lys Ala Tyr Gly Ser
   2850                2855                2860

ggg gcc gat ggg gtc ggc tgg gcc gag ggt gtg ggt gtg ctg ttg gtg   8640
Gly Ala Asp Gly Val Gly Trp Ala Glu Gly Val Gly Val Leu Leu Val
2865                2870                2875                2880

gag cgg ctg tcc gag gct gaa cgt cgt ggt cat cgg gtt ttg gcg gtg   8688
Glu Arg Leu Ser Glu Ala Glu Arg Arg Gly His Arg Val Leu Ala Val
               2885                2890                2895

gtg cgg ggg agt gcg gtg aat cag gac ggt gcg tcg aat ggg ttg acg   8736
Val Arg Gly Ser Ala Val Asn Gln Asp Gly Ala Ser Asn Gly Leu Thr
           2900                2905                2910

gcg ccg aat ggt ccg tcg cag cag cgg gtg att cgg cag gcg ttg gcg   8784
Ala Pro Asn Gly Pro Ser Gln Gln Arg Val Ile Arg Gln Ala Leu Ala
       2915                2920                2925

tgt gcg ggg ttg tcc gtg gcg gat gtg gat gtg gtg gag ggg cac ggg   8832
Cys Ala Gly Leu Ser Val Ala Asp Val Asp Val Val Glu Gly His Gly
   2930                2935                2940

acg ggt acg acg ttg ggt gat ccg atc gag gcg cag gcg ttg ctc gcc   8880
Thr Gly Thr Thr Leu Gly Asp Pro Ile Glu Ala Gln Ala Leu Leu Ala
2945                2950                2955                2960

acg tac ggg cag ggt cgt tcg ggg gag cgg ccg gtg tgg ttg ggg tcg   8928
Thr Tyr Gly Gln Gly Arg Ser Gly Glu Arg Pro Val Trp Leu Gly Ser
               2965                2970                2975

gtg aag tcg aac atc ggg cat gcg cag gct gcc gcg ggt gtg gcc ggt   8976
Val Lys Ser Asn Ile Gly His Ala Gln Ala Ala Ala Gly Val Ala Gly
           2980                2985                2990
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gtg atc aag atg gtc atg gcc ctg aac cac gaa ctg ttg ccg acc agc   9024
Val Ile Lys Met Val Met Ala Leu Asn His Glu Leu Leu Pro Thr Ser
       2995                3000                3005

ctg cac atc gac gaa ccc tcc ccc cac atc gac tgg tcg agc ggc ggc   9072
Leu His Ile Asp Glu Pro Ser Pro His Ile Asp Trp Ser Ser Gly Gly
   3010                3015                3020

gtc cgg ctt ctc acc gag ccc gta ccg tgg cag cag aac ggc cgg ccc   9120
Val Arg Leu Leu Thr Glu Pro Val Pro Trp Gln Gln Asn Gly Arg Pro
3025                3030                3035                3040

agg cgc gcg ggc gtc tcc gcg ttc gga gtc agc ggg acc aac gcc cac   9168
Arg Arg Ala Gly Val Ser Ala Phe Gly Val Ser Gly Thr Asn Ala His
               3045                3050                3055

gtc atc atc gag cag gcg ccg gtc gag gcg cac gtc atc agt gag ccg   9216
Val Ile Ile Glu Gln Ala Pro Val Glu Ala His Val Ile Ser Glu Pro
           3060                3065                3070

gta ccg gct gag gcg cac gtc atc gtc gag cag gcg ccg gtc gag gcg   9264
Val Pro Ala Glu Ala His Val Ile Val Glu Gln Ala Pro Val Glu Ala
       3075                3080                3085

ccc cac gtg gtc gac gcc acc gga ccg gcg gac ctc acc gag ccg caa   9312
Pro His Val Val Asp Ala Thr Gly Pro Ala Asp Leu Thr Glu Pro Gln
   3090                3095                3100

gag gag gcg gct gaa ccg gag tgc gtc gct gac gcc gtg acc gag atg   9360
Glu Glu Ala Ala Glu Pro Glu Cys Val Ala Asp Ala Val Thr Glu Met
3105                3110                3115                3120

tcg gct gaa ccg gag tgc gtc gcc gac gcc atg tcc gag atg tcg gct   9408
Ser Ala Glu Pro Glu Cys Val Ala Asp Ala Met Ser Glu Met Ser Ala
               3125                3130                3135

gag tgc gtc gcc gag gcc gtg tcc gac aag tcg gct gaa ccg gag tgc   9456
Glu Cys Val Ala Glu Ala Val Ser Asp Lys Ser Ala Glu Pro Glu Cys
           3140                3145                3150

gtc gcc gac gcc atg tcc gac aag ccg gcc ctc ctg ccc atc ccg tgg   9504
Val Ala Asp Ala Met Ser Asp Lys Pro Ala Leu Leu Pro Ile Pro Trp
       3155                3160                3165

ctg ctc tcc gcc aag tcc gag cga gcg ctg cgg ggc cag gcg cga cgg   9552
Leu Leu Ser Ala Lys Ser Glu Arg Ala Leu Arg Gly Gln Ala Arg Arg
   3170                3175                3180

ttg cgg cag ttc gct gcc agg gca tcc gat gcc cgg ccg gcc gac gtg   9600
Leu Arg Gln Phe Ala Ala Arg Ala Ser Asp Ala Arg Pro Ala Asp Val
3185                3190                3195                3200

gcg cac gcc ctg gcg gca cag cgg tcc gtg ttc gat cac cgg gcc gtc   9648
Ala His Ala Leu Ala Ala Gln Arg Ser Val Phe Asp His Arg Ala Val
               3205                3210                3215

gtc gtg gcc gag gac cgc gac ggc ttc ctt cag gcc ctc gac gcg ctg   9696
Val Val Ala Glu Asp Arg Asp Gly Phe Leu Gln Ala Leu Asp Ala Leu
           3220                3225                3230
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gcc gag ggc cgg tcg gcg gac ggc ctg atc gaa ggg tcg gtc ggc ccg   9744
Ala Glu Gly Arg Ser Ala Asp Gly Leu Ile Glu Gly Ser Val Gly Pro
       3235                3240                3245

cgt ggc ggc cac tca ggc cgc cgg cgc gga aag acc gcc atg ctg ttc   9792
Arg Gly Gly His Ser Gly Arg Arg Arg Gly Lys Thr Ala Met Leu Phe
   3250                3255                3260

gcc gga cag ggc acg caa cgc gtg gga atg ggc cgt cag ctg tat gcg   9840
Ala Gly Gln Gly Thr Gln Arg Val Gly Met Gly Arg Gln Leu Tyr Ala
3265                3270                3275                3280

gct cac ccg gcc tac gcg gac gcg ctg gac cag gta ctg gcg gaa ctg   9888
Ala His Pro Ala Tyr Ala Asp Ala Leu Asp Gln Val Leu Ala Glu Leu
               3285                3290                3295

gac ggt cac ctg gac cag ccc ctg cgc ccg ctg atc cac gcc agt gcg   9936
Asp Gly His Leu Asp Gln Pro Leu Arg Pro Leu Ile His Ala Ser Ala
           3300                3305                3310

gat ctt gcg gat gtc gcg gat gcc gcg gat gtt ctg gac cgt acg cgg   9984
Asp Leu Ala Asp Val Ala Asp Ala Ala Asp Val Leu Asp Arg Thr Arg
       3315                3320                3325

tac gcc cag ccg gcg ctg ttc gcc gtc cag gtc gcg ctc ttc cgg cac  10032
Tyr Ala Gln Pro Ala Leu Phe Ala Val Gln Val Ala Leu Phe Arg His
   3330                3335                3340

ctg gaa cgt ctc ggc gtg cgc gcg gac ttc gtg gcc ggg cac tcg atc  10080
Leu Glu Arg Leu Gly Val Arg Ala Asp Phe Val Ala Gly His Ser Ile
3345                3350                3355                3360

ggc gag ctc gcg gcc gcc cac gtc gcc ggg gtg ctt ccc ctg gca gca  10128
Gly Glu Leu Ala Ala Ala His Val Ala Gly Val Leu Pro Leu Ala Ala
               3365                3370                3375

gcc tgc cgc ctg gtg gcg gcc cgc ggg cgc ctg atg gag cag ctc gca  10176
Ala Cys Arg Leu Val Ala Ala Arg Gly Arg Leu Met Glu Gln Leu Ala
           3380                3385                3390

cca ggc ggc gcc atg gtc gcc gta cgg gcg agc gaa gcc gag gcg cga  10224
Pro Gly Gly Ala Met Val Ala Val Arg Ala Ser Glu Ala Glu Ala Arg
       3395                3400                3405

cag gcg ctc gac ggc cgg gaa gcc cgg gtg tcg gtc gcg gcc gtg aac  10272
Gln Ala Leu Asp Gly Arg Glu Ala Arg Val Ser Val Ala Ala Val Asn
   3410                3415                3420

gga ccc gcc tcg gtg gtg ttc tcc ggc gcc gag gac gag gtg ggg aac  10320
Gly Pro Ala Ser Val Val Phe Ser Gly Ala Glu Asp Glu Val Gly Asn
3425                3430                3435                3440

atg gcg gac tgg ttc gcc gag cgc ggg cgg aga gtc aag cgc ctg cga  10368
Met Ala Asp Trp Phe Ala Glu Arg Gly Arg Arg Val Lys Arg Leu Arg
               3445                3450                3455

acc ggg cat gcc ttc cac tca ccg ctg atg gac ccg atg ctg gag gag  10416
Thr Gly His Ala Phe His Ser Pro Leu Met Asp Pro Met Leu Glu Glu
           3460                3465                3470
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ttc cag cag gtc gcg gcc tcg ctg acc tac agc gaa cca gcc att ccc   10464
Phe Gln Gln Val Ala Ala Ser Leu Thr Tyr Ser Glu Pro Ala Ile Pro
       3475                3480                3485

atg gtg tcg acg ctc acc ggc gac atc gtg gcg gcg gga gaa ctg agc   10512
Met Val Ser Thr Leu Thr Gly Asp Ile Val Ala Ala Gly Glu Leu Ser
   3490                3495                3500

gac ccc gag tac tgg gtc cgg cag gta cgg cgg acc gtg cgc ttc ggc   10560
Asp Pro Glu Tyr Trp Val Arg Gln Val Arg Arg Thr Val Arg Phe Gly
3505                3510                3515                3520

gac gcg atc agc cgc ctg cac acc gac gga gtc cgc acc ttc atg gaa   10608
Asp Ala Ile Ser Arg Leu His Thr Asp Gly Val Arg Thr Phe Met Glu
               3525                3530                3535

ctg ggc cca gac ggg acc ctg tcg gca ctg gcc gag gaa tgc cta gag   10656
Leu Gly Pro Asp Gly Thr Leu Ser Ala Leu Ala Glu Glu Cys Leu Glu
           3540                3545                3550

gcc acc gcc gac agc cac ccc gcc gac gac gac acc ggc acc ccg caa   10704
Ala Thr Ala Asp Ser His Pro Ala Asp Asp Asp Thr Gly Thr Pro Gln
       3555                3560                3565

gag aac ctg ctc atc ccg ctc cta cgg ccg gac agc ccg gaa ccc ggc   10752
Glu Asn Leu Leu Ile Pro Leu Leu Arg Pro Asp Ser Pro Glu Pro Gly
   3570                3575                3580

acc ctg ctc acc ggc ttg gcc cgg ctg cat acg cac gga gcg gcg gcg   10800
Thr Leu Leu Thr Gly Leu Ala Arg Leu His Thr His Gly Ala Ala Ala
3585                3590                3595                3600

gtc aac tgg ccc gcc gcc ctg ccc gaa cgc gat cga gcc cgc cac ctc   10848
Val Asn Trp Pro Ala Ala Leu Pro Glu Arg Asp Arg Ala Arg His Leu
               3605                3610                3615

gac ctg ccg acc tac gcc ttc gat cac cac cgc tac tgg gtc gac acc   10896
Asp Leu Pro Thr Tyr Ala Phe Asp His His Arg Tyr Trp Val Asp Thr
           3620                3625                3630

tcg gcc ggc cac ccg ggg gac ctg tcg gca gcg ggg ctc ggc acc gcc   10944
Ser Ala Gly His Pro Gly Asp Leu Ser Ala Ala Gly Leu Gly Thr Ala
       3635                3640                3645

ggg cat ccc ctg ctc ggt tcc gcg gtg gca ctg gcc gag tcg cag gaa   10992
Gly His Pro Leu Leu Gly Ser Ala Val Ala Leu Ala Glu Ser Gln Glu
   3650                3655                3660

ctc ctc ttc acc ggc cgt ctc tcc ctg cgc aca cac ccg tgg ctg gcc   11040
Leu Leu Phe Thr Gly Arg Leu Ser Leu Arg Thr His Pro Trp Leu Ala
3665                3670                3675                3680

gac cac gcc atc ttc ggt acc gtc ctg ctg ccc ggc acg gcc atc ctg   11088
Asp His Ala Ile Phe Gly Thr Val Leu Leu Pro Gly Thr Ala Ile Leu
               3685                3690                3695

gaa ctg gcc gtg cgc gca ggc gac gag gtc gac tgc ggc acc gtc gag   11136
Glu Leu Ala Val Arg Ala Gly Asp Glu Val Asp Cys Gly Thr Val Glu
           3700                3705                3710
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gaa ctc acc ctg cgg aca ccg ctc gtc ctt ccc gaa cag ggc tcg gtg   11184
Glu Leu Thr Leu Arg Thr Pro Leu Val Leu Pro Glu Gln Gly Ser Val
       3715                3720                3725

atc ctg caa ctc tcc gtc ggg gca ccc cag ggc ccc cag acg ccc gag   11232
Ile Leu Gln Leu Ser Val Gly Ala Pro Gln Gly Pro Gln Thr Pro Glu
   3730                3735                3740

gag ccc gaa cgg cgc acc ttc gcc ctg tac gcc cgc gaa gac gac gga   11280
Glu Pro Glu Arg Arg Thr Phe Ala Leu Tyr Ala Arg Glu Asp Asp Gly
3745                3750                3755                3760

ctg tcg tcc tcg tcc gcg gcg gcg acc ggc acc gag tgg acc tgc cac   11328
Leu Ser Ser Ser Ser Ala Ala Ala Thr Gly Thr Glu Trp Thr Cys His
               3765                3770                3775

gcc acc ggc gtc ctg acc ggc acc gcc cgg ccc gcg gag gag cac aca   11376
Ala Thr Gly Val Leu Thr Gly Thr Ala Arg Pro Ala Glu Glu His Thr
           3780                3785                3790

cag gaa ccg tgg ccg ccc gcc gac gca gca ccg gtg gac ctg gac ggc   11424
Gln Glu Pro Trp Pro Pro Ala Asp Ala Ala Pro Val Asp Leu Asp Gly
       3795                3800                3805

tgg tac gag cag ctg gcc ggc gcc ggc ctg gga tac ggg ccg gtg ttc   11472
Trp Tyr Glu Gln Leu Ala Gly Ala Gly Leu Gly Tyr Gly Pro Val Phe
   3810                3815                3820

cag ggg ctg cgc gag gtc tgg cgg cgc ggg gac gag gtg ttc gcc gtc   11520
Gln Gly Leu Arg Glu Val Trp Arg Arg Gly Asp Glu Val Phe Ala Val
3825                3830                3835                3840

gtc acc ctg ccc gag agc acg gag gga cag gcg gcc gac gcc gcc cgg   11568
Val Thr Leu Pro Glu Ser Thr Glu Gly Gln Ala Ala Asp Ala Ala Arg
               3845                3850                3855

tac gcc ctg cac ccg gcc ctg ctg gac gcg gca ctg cac ccg gtc gtt   11616
Tyr Ala Leu His Pro Ala Leu Leu Asp Ala Ala Leu His Pro Val Val
           3860                3865                3870

ctg cgc cac gag ggc gat gcc gcc gcc gac gga cac ggc tgg ctg ccg   11664
Leu Arg His Glu Gly Asp Ala Ala Ala Asp Gly His Gly Trp Leu Pro
       3875                3880                3885

ttc tcc tgg acc ggc gtc acg gtc gcc gcc tcc ggc gcc tcc acc ctg   11712
Phe Ser Trp Thr Gly Val Thr Val Ala Ala Ser Gly Ala Ser Thr Leu
   3890                3895                3900

cac gtc cgt ctc acc gtc cgc acg gac gag gac gcg gtc gga ctg ctg   11760
His Val Arg Leu Thr Val Arg Thr Asp Glu Asp Ala Val Gly Leu Leu
3905                3910                3915                3920

gcc acc gac gca tcg gga cgc atc gtc atc tcc gcg ggg tcc ctc gcc   11808
Ala Thr Asp Ala Ser Gly Arg Ile Val Ile Ser Ala Gly Ser Leu Ala
               3925                3930                3935

ttc cgg ccc gtc tcc gcc gag cag ctc cag gcc gcg cgc acc ggc tac   11856
Phe Arg Pro Val Ser Ala Glu Gln Leu Gln Ala Ala Arg Thr Gly Tyr
           3940                3945                3950
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cac gac cac ctc ttc cgc atc gaa tgg cgg ccg ctg cac ctc ccc acc   11904
His Asp His Leu Phe Arg Ile Glu Trp Arg Pro Leu His Leu Pro Thr
       3955                3960                3965

aca ccg gca cgg aca gcc gac tgg gcc cta atc ggc ccc ggt gcc cgg   11952
Thr Pro Ala Arg Thr Ala Asp Trp Ala Leu Ile Gly Pro Gly Ala Arg
   3970                3975                3980

cgg acg gcc gcc gtc ctg gag cgc aac ggc gcc tcc tgg cag gcc tac   12000
Arg Thr Ala Ala Val Leu Glu Arg Asn Gly Ala Ser Trp Gln Ala Tyr
3985                3990                3995                4000

ccg gac ccg gcg gct ctc gca gaa gcc ctg gcg gcc ggc gcc ccg gca   12048
Pro Asp Pro Ala Ala Leu Ala Glu Ala Leu Ala Ala Gly Ala Pro Ala
               4005                4010                4015

ccg ggc atg gtc gtc atc tcg tgc gag ccg gac ggc gca tcc gcc ccc   12096
Pro Gly Met Val Val Ile Ser Cys Glu Pro Asp Gly Ala Ser Ala Pro
           4020                4025                4030

acc gat tcc gcc ctc acc gat tcc gcc ctc acc gat tcc gcc ccg gcc   12144
Thr Asp Ser Ala Leu Thr Asp Ser Ala Leu Thr Asp Ser Ala Pro Ala
       4035                4040                4045

ggc tcg gcc ccg gcc gac tcc acc gcc ctc gcc gac gcc acc cgg caa   12192
Gly Ser Ala Pro Ala Asp Ser Thr Ala Leu Ala Asp Ala Thr Arg Gln
   4050                4055                4060

gcc acc acc cgc gtc ctc gcc ctg ctc cag gaa tgg gtc gcc gac gaa   12240
Ala Thr Thr Arg Val Leu Ala Leu Leu Gln Glu Trp Val Ala Asp Glu
4065                4070                4075                4080

cgg ctc gcg gcc tgc cgc ctg gcc ctc ctc acg cac ggc tcg gtc acc   12288
Arg Leu Ala Ala Cys Arg Leu Ala Leu Leu Thr His Gly Ser Val Thr
               4085                4090                4095

gcg acc ccc gac gag ccc gtg tcc gac ctc gca cac gcc gcc gtc tgg   12336
Ala Thr Pro Asp Glu Pro Val Ser Asp Leu Ala His Ala Ala Val Trp
           4100                4105                4110

gga ctg gtc cgc tcc gtg cag acc gag aac ccc gac cgg ttc ctg ctg   12384
Gly Leu Val Arg Ser Val Gln Thr Glu Asn Pro Asp Arg Phe Leu Leu
       4115                4120                4125

gcc gac acc gac gac acc gac gcc tcc cgc aac gcc ctt ccc ctg ctg   12432
Ala Asp Thr Asp Asp Thr Asp Ala Ser Arg Asn Ala Leu Pro Leu Leu
   4130                4135                4140

gcc ggg gaa ccg cag atc gcc ctg cga aat ggt gcc gtc cgc atc ccg   12480
Ala Gly Glu Pro Gln Ile Ala Leu Arg Asn Gly Ala Val Arg Ile Pro
4145                4150                4155                4160

cgg atg aca cga gtg ccc gtc cgg cag cca cag ccg agc acc acc gac   12528
Arg Met Thr Arg Val Pro Val Arg Gln Pro Gln Pro Ser Thr Thr Asp
               4165                4170                4175

gcc gac tgg gac ccg gag gcc acg gtc ctc atc acg ggc ggt acc ggc   12576
Ala Asp Trp Asp Pro Glu Ala Thr Val Leu Ile Thr Gly Gly Thr Gly
           4180                4185                4190
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gtc ctc ggc cgg ctc gtc gcc cgt cat ctc gcc acg gcc cac ggg gta   12624
Val Leu Gly Arg Leu Val Ala Arg His Leu Ala Thr Ala His Gly Val
       4195                4200                4205

cgg cac ctg ctg ctg gcc acc cgc cgc ggc acg gcc gcg gac ggc gcc   12672
Arg His Leu Leu Leu Ala Thr Arg Arg Gly Thr Ala Ala Asp Gly Ala
   4210                4215                4220

gcc gac ctg gtc gcc gaa ctc gcc ggc ctc ggc gcc gag gcc acg gtc   12720
Ala Asp Leu Val Ala Glu Leu Ala Gly Leu Gly Ala Glu Ala Thr Val
4225                4230                4235                4240

gcg gcc tgc gac atc ggg gac cgg gcg gcc gtc gcc gcg ctc ctc gac   12768
Ala Ala Cys Asp Ile Gly Asp Arg Ala Ala Val Ala Ala Leu Leu Asp
               4245                4250                4255

caa gtg ccc gcg cag cac ccc ctg aaa gcc gtg atc cac acg gcc ggt   12816
Gln Val Pro Ala Gln His Pro Leu Lys Ala Val Ile His Thr Ala Gly
           4260                4265                4270

gtg gtc gac gac ggc atc ctc acc tcg ctc act ccg gag cgc atg gag   12864
Val Val Asp Asp Gly Ile Leu Thr Ser Leu Thr Pro Glu Arg Met Glu
       4275                4280                4285

gcc gtc ctg cac gcg aag gcg ttc ggc gcc gcg cac ctg cac gac ctg   12912
Ala Val Leu His Ala Lys Ala Phe Gly Ala Ala His Leu His Asp Leu
   4290                4295                4300

acc cgc gac gcc ggc ctc acc acc ttc acc gtc ttc tcc tcg gcc gcc   12960
Thr Arg Asp Ala Gly Leu Thr Thr Phe Thr Val Phe Ser Ser Ala Ala
4305                4310                4315                4320

gcc tcc ttc ggc agt ccc gga cag ggc aac tac acc gcg gcg aac gcc   13008
Ala Ser Phe Gly Ser Pro Gly Gln Gly Asn Tyr Thr Ala Ala Asn Ala
               4325                4330                4335

ttt ctg gac gcc ctg atg cag cac cgc cac acc cag gca ctg ccg ggc   13056
Phe Leu Asp Ala Leu Met Gln His Arg His Thr Gln Ala Leu Pro Gly
           4340                4345                4350

cgg tcg ctc gcc tgg ggc ctt tgg ggc gag gcc gac ggc atg acc cgc   13104
Arg Ser Leu Ala Trp Gly Leu Trp Gly Glu Ala Asp Gly Met Thr Arg
       4355                4360                4365

aac ctc gcc ggc acc gac ttc gcg cgc atg gcc cgc ggc ggc ctg ctc   13152
Asn Leu Ala Gly Thr Asp Phe Ala Arg Met Ala Arg Gly Gly Leu Leu
   4370                4375                4380

ccc ctg tcc aac gca cag gga ctc gcg ctc ctc gac aca gcg gat cgc   13200
Pro Leu Ser Asn Ala Gln Gly Leu Ala Leu Leu Asp Thr Ala Asp Arg
4385                4390                4395                4400

ctc ggc cct ttc ggt gac ggg ctg ctc ctc gcc acc cgg ctc gac gcg   13248
Leu Gly Pro Phe Gly Asp Gly Leu Leu Leu Ala Thr Arg Leu Asp Ala
               4405                4410                4415

gcc acc ctc cac gca cag gcc acg gcc ggc gcc ctg ccg cgc atc ctg   13296
Ala Thr Leu His Ala Gln Ala Thr Ala Gly Ala Leu Pro Arg Ile Leu
           4420                4425                4430
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Replacement Sheet

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cac ggg ctg atc cgc atc ccg gcc cgg cgg tcc gcc gac cac ggc atc   13344
His Gly Leu Ile Arg Ile Pro Ala Arg Arg Ser Ala Asp His Gly Ile
       4435                4440                4445

gcg acc gac acc ccc gcc acg ctg cgc gag cgc ctg gcc gga ctc acc   13392
Ala Thr Asp Thr Pro Ala Thr Leu Arg Glu Arg Leu Ala Gly Leu Thr
   4450                4455                4460

atc ccc gcg cag cgc acc ggt ctc ctc ctg gaa ctc gta cgg acc cat   13440
Ile Pro Ala Gln Arg Thr Gly Leu Leu Leu Glu Leu Val Arg Thr His
4465                4470                4475                4480

gcc gcc gcc gtc ctc ggc cac ccc acc agc gcc gtc aca gcc gcg gac   13488
Ala Ala Ala Val Leu Gly His Pro Thr Ser Ala Val Thr Ala Ala Asp
               4485                4490                4495

ggc gca ctc ccg gac gat ctg gtc ccg gcc gac acc gag ttc cgc gac   13536
Gly Ala Leu Pro Asp Asp Leu Val Pro Ala Asp Thr Glu Phe Arg Asp
           4500                4505                4510

ctc ggc ttc gac tcg ctg acc gcc gtc gaa ctc cgc aac cgg atc aac   13584
Leu Gly Phe Asp Ser Leu Thr Ala Val Glu Leu Arg Asn Arg Ile Asn
       4515                4520                4525

gcc gtc acc ggc ctg cgc ctc ccg gca acg ctc atc ttc gac cag ccc   13632
Ala Val Thr Gly Leu Arg Leu Pro Ala Thr Leu Ile Phe Asp Gln Pro
   4530                4535                4540

agc ccc gcg gca ctc gcc gat cac ctc gcg acc cgc ctg acg gcc gag   13680
Ser Pro Ala Ala Leu Ala Asp His Leu Ala Thr Arg Leu Thr Ala Glu
4545                4550                4555                4560

gcg ggc acg ccg gac gag ccg gcc cct gcc gcc gcg gca gcc ggg gcc   13728
Ala Gly Thr Pro Asp Glu Pro Ala Pro Ala Ala Ala Ala Ala Gly Ala
               4565                4570                4575

ggg agc gca ggg agt gcc gag acc gga cag cag cgc agt acg ggg agc   13776
Gly Ser Ala Gly Ser Ala Glu Thr Gly Gln Gln Arg Ser Thr Gly Ser
           4580                4585                4590

gag aag cag cag acc agg ggc ggc acc tcc acc gaa acc gtc gaa tcc   13824
Glu Lys Gln Gln Thr Arg Gly Gly Thr Ser Thr Glu Thr Val Glu Ser
       4595                4600                4605

ctg ttc tgg atc gga cac gac acc cgc cgc atc gag gag tcc atg gcc   13872
Leu Phe Trp Ile Gly His Asp Thr Arg Arg Ile Glu Glu Ser Met Ala
   4610                4615                4620

ctg ctc tcg gcg gcc tcc ttc ttc cgg ccc gcc ttc acg gac ccc tcg   13920
Leu Leu Ser Ala Ala Ser Phe Phe Arg Pro Ala Phe Thr Asp Pro Ser
4625                4630                4635                4640

gac atc ccg gag ccg acg ttc gtc cgg ctc gcc cag ggt gaa gcg cgc   13968
Asp Ile Pro Glu Pro Thr Phe Val Arg Leu Ala Gln Gly Glu Ala Arg
               4645                4650                4655

gcc caa ggt gaa gca ctc gcc cgg ggc gaa aca cgg ccc gcc ctc atc   14016
Ala Gln Gly Glu Ala Leu Ala Arg Gly Glu Thr Arg Pro Ala Leu Ile
           4660                4665                4670
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tgc ctg ccc acc gtc gcc gcc gtg tcg agc gtg tac cag tac tca cgt   14064
Cys Leu Pro Thr Val Ala Ala Val Ser Ser Val Tyr Gln Tyr Ser Arg
       4675                4680                4685

ttc gcg gcg gga ctg aac gga cac cga gac gtc tgg tac gtt cct gcg   14112
Phe Ala Ala Gly Leu Asn Gly His Arg Asp Val Trp Tyr Val Pro Ala
   4690                4695                4700

cca ggg ttc ctg gag ggc gaa ccc ctg ccg tcc gga atc ggc gcg gtg   14160
Pro Gly Phe Leu Glu Gly Glu Pro Leu Pro Ser Gly Ile Gly Ala Val
4705                4710                4715                4720

acc cgc atg ttc gcc gac gcg atc gtc cgg ttc acc gac ggc gcg cct   14208
Thr Arg Met Phe Ala Asp Ala Ile Val Arg Phe Thr Asp Gly Ala Pro
       -        4725                4730                4735

ttt gcg ctc gcc ggg cat tcc gcg ggc gga tgg ttc gtc tac gcg gtg   14256
Phe Ala Leu Ala Gly His Ser Ala Gly Gly Trp Phe Val Tyr Ala Val
           4740                4745                4750

acg agt cat ctg gag cgt cta ggc gtc cgt ccg gaa gcg gtg gtg acc   14304
Thr Ser His Leu Glu Arg Leu Gly Val Arg Pro Glu Ala Val Val Thr
       4755                4760                4765

atg gac gcc tat ctc ccg gac gac ggc atc gca cct gtc gcg tcc gcg   14352
Met Asp Ala Tyr Leu Pro Asp Asp Gly Ile Ala Pro Val Ala Ser Ala
   4770                4775                4780

ctg aca agt gaa atc ttc gac cgc gtc acg cag ttt gtg gac gtg gac   14400
Leu Thr Ser Glu Ile Phe Asp Arg Val Thr Gln Phe Val Asp Val Asp
4785                4790                4795                4800

tac aca cgc ctg gtc gcc atg ggc gga tac ttc cgc atc ttc tcc ggc   14448
Tyr Thr Arg Leu Val Ala Met Gly Gly Tyr Phe Arg Ile Phe Ser Gly
               4805                4810                4815

tgg agt cct ccg gac atc acc aca ccc gcc ctc ttc ctg cgc ggc cgg   14496
Trp Ser Pro Pro Asp Ile Thr Thr Pro Ala Leu Phe Leu Arg Gly Arg
           4820                4825                4830

gac gga gaa cag atg ccg ccg ccg tgg gga gtt ccg cac acc gtt ctg   14544
Asp Gly Glu Gln Met Pro Pro Pro Trp Gly Val Pro His Thr Val Leu
       4835                4840                4845

gac atc cag ggg aat cac ttc acg atg ctg gaa cag ttt gcg gat tcg   14592
Asp Ile Gln Gly Asn His Phe Thr Met Leu Glu Gln Phe Ala Asp Ser
   4850                4855                4860

act gct cgg cat gtc gac gaa tgg ctg aca gaa atc gca tca gtg cgg   14640
Thr Ala Arg His Val Asp Glu Trp Leu Thr Glu Ile Ala Ser Val Arg
4865                4870                4875                4880

cgc tgatcgcgcc tctgatcgcg gtcctgatcg cggccctgat cggcgggtcg        14693
Arg

ggcacagccc ggtcggccgg tcggccagtc ggccagtcgg tggtatccgg tcggctccgg 14753

catcgatcag tgctttcccc cttacggcca tacgggcctt tctgagactt cttgaatttg 14813
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ggagacagtg atg gac acg tcc agc gaa aag ctc gtc gac gcg ctt agg    14862
           Met Asp Thr Ser Ser Glu Lys Leu Val Asp Ala Leu Arg
                       4885                4890

gcg tct ctg aag gcg aac cag acc ctg cgg gca cgt aat gag caa ctg   14910
Ala Ser Leu Lys Ala Asn Gln Thr Leu Arg Ala Arg Asn Glu Gln Leu
4895              4900                4905                4910

gca gcc gcc atg gag gcg tcc agc gag ccg att gcg att gtg ggg atg   14958
Ala Ala Ala Met Glu Ala Ser Ser Glu Pro Ile Ala Ile Val Gly Met
               4915                4920                4925

gcg tgt cgt ttt ccg ggt ggg gtg tgt tcg ccg gag gag ttg tgg gag   15006
Ala Cys Arg Phe Pro Gly Gly Val Cys Ser Pro Glu Glu Leu Trp Glu
           4930                4935                4940

ctg gtt gcg tcg ggt ggg gat gcg att ggt gaa ttt ccg gcc ggt cgg   15054
Leu Val Ala Ser Gly Gly Asp Ala Ile Gly Glu Phe Pro Ala Gly Arg
       4945                4950                4955

ggg tgg gat ctg gag ggg ttg ttt gat tcg gac cct gac cgg tcg ggg   15102
Gly Trp Asp Leu Glu Gly Leu Phe Asp Ser Asp Pro Asp Arg Ser Gly
   4960                4965                4970

acg tcg tac gcg cgg tat ggc ggg ttt ttg tat gag gcg ggg gag ttc   15150
Thr Ser Tyr Ala Arg Tyr Gly Gly Phe Leu Tyr Glu Ala Gly Glu Phe
4975              4980                4985                4990

gat gcg gac ttc ttc ggg atc agt ccg cgt gag gcg ttg gcg atg gat   15198
Asp Ala Asp Phe Phe Gly Ile Ser Pro Arg Glu Ala Leu Ala Met Asp
               4995                5000                5005

ccg cag cag cgg ttg ttg ctg gag acg tcg tgg gag gcg ttc gag cgg   15246
Pro Gln Gln Arg Leu Leu Leu Glu Thr Ser Trp Glu Ala Phe Glu Arg
           5010                5015                5020

gcg ggt atc gat ccg ctg tcg atg cgt ggc tcc cgt acg ggt gtc ttc   15294
Ala Gly Ile Asp Pro Leu Ser Met Arg Gly Ser Arg Thr Gly Val Phe
       5025                5030                5035

gcc ggg gtg atg tac cac gac tac gga tcc cgc ctg ggt acc atc ccc   15342
Ala Gly Val Met Tyr His Asp Tyr Gly Ser Arg Leu Gly Thr Ile Pro
   5040                5045                5050

gag gga ttc gag ggc tac atc ggc aac ggt agc ggc ggc gcc gtc gcg   15390
Glu Gly Phe Glu Gly Tyr Ile Gly Asn Gly Ser Gly Gly Ala Val Ala
5055              5060                5065                5070

tcg ggc cgc gtc gcc tac acg ctc ggt ctc gag ggc cct gcc gtc tcg   15438
Ser Gly Arg Val Ala Tyr Thr Leu Gly Leu Glu Gly Pro Ala Val Ser
               5075                5080                5085

gtg gac acg gca tgt tcg tcg tcg ttg gtg gcg ctg cat ctg gcg tgc   15486
Val Asp Thr Ala Cys Ser Ser Ser Leu Val Ala Leu His Leu Ala Cys
           5090                5095                5100

cag tcg ctg cgg tcg ggt gag tgc acg ctc gcg ctg gcc ggc ggt gtg   15534
Gln Ser Leu Arg Ser Gly Glu Cys Thr Leu Ala Leu Ala Gly Gly Val
       5105                5110                5115
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Replacement Sheet

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acg gtg atg tcg acc ccg cac ctc ttc gtc gag ttc tca cgc cag cgc   15582
Thr Val Met Ser Thr Pro His Leu Phe Val Glu Phe Ser Arg Gln Arg
   5120                5125                5130

gga ctg tcg gtg gac ggc cgc tgc aag tcc ttc gcg ggt gga gcc gac   15630
Gly Leu Ser Val Asp Gly Arg Cys Lys Ser Phe Ala Gly Gly Ala Asp
5135                5140                5145                5150

ggc acc ggc atg ggc gag ggc gtc ggg atg ctg ttg gtg gag cgg ttg   15678
Gly Thr Gly Met Gly Glu Gly Val Gly Met Leu Leu Val Glu Arg Leu
               5155                5160                5165

tcg gat gcg gtg cgg ctg ggg cat cgg gtg ctg gcg gtg ctg cgc ggc   15726
Ser Asp Ala Val Arg Leu Gly His Arg Val Leu Ala Val Leu Arg Gly
           5170                5175                5180

agt gcg gtc aat cag gac ggt gcg tcg aat ggg ttg acg gcg ccg aat   15774
Ser Ala Val Asn Gln Asp Gly Ala Ser Asn Gly Leu Thr Ala Pro Asn
       5185                5190                5195

ggt ccg gct cag gag cgg gtg atc cgg cag gcg ttg gcg aac gcg ggg   15822
Gly Pro Ala Gln Glu Arg Val Ile Arg Gln Ala Leu Ala Asn Ala Gly
   5200                5205                5210

ttg tcc gtg gcg gat gtg gat gtg gtg gag ggg cat ggg acg ggc acg   15870
Leu Ser Val Ala Asp Val Asp Val Val Glu Gly His Gly Thr Gly Thr
5215                5220                5225                5230

acg ctg ggt gat ccg atc gag gcg cag gcg ttg ctc gcc acg tac ggg   15918
Thr Leu Gly Asp Pro Ile Glu Ala Gln Ala Leu Leu Ala Thr Tyr Gly
               5235                5240                5245

cag cgg gcc ggt aac agg ccg ctg tgg ctg gga tcg gtg aag tcg aac   15966
Gln Arg Ala Gly Asn Arg Pro Leu Trp Leu Gly Ser Val Lys Ser Asn
           5250                5255                5260

atc ggc cat gcg cag gct gcc gcg ggt gtg ggt ggg gtc atc aag atg   16014
Ile Gly His Ala Gln Ala Ala Ala Gly Val Gly Gly Val Ile Lys Met
       5265                5270                5275

gtg atg gcg ttg cgg gag ggg gtg ttg ccg cgg acg ttg cat gtg gat   16062
Val Met Ala Leu Arg Glu Gly Val Leu Pro Arg Thr Leu His Val Asp
   5280                5285                5290

gag ccg tcg ccg cag gtg gac tgg tcc gcg ggg gcg gtg cgg ctg ctg   16110
Glu Pro Ser Pro Gln Val Asp Trp Ser Ala Gly Ala Val Arg Leu Leu
5295                5300                5305                5310

acg gag gcg gtg ccg tgg ccg ggg gac gcg gca ggg cgg ttg cgg cgg   16158
Thr Glu Ala Val Pro Trp Pro Gly Asp Ala Ala Gly Arg Leu Arg Arg
               5315                5320                5325

gcg gga gtg tcg tcg ttc ggg gtc agt ggc acg aat gcg cat gtg att   16206
Ala Gly Val Ser Ser Phe Gly Val Ser Gly Thr Asn Ala His Val Ile
           5330                5335                5340

ttg gag gag gcg ccg gcg gcg ggg ggc tgt gtt gcc ggg ggt ggg gtg   16254
Leu Glu Glu Ala Pro Ala Ala Gly Gly Cys Val Ala Gly Gly Gly Val
       5345                5350                5355
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ttg gag ggt gct ccg ggt ctt gcc att tcg gtg gct gag tcg gtg gcc 16302
Leu Glu Gly Ala Pro Gly Leu Ala Ile Ser Val Ala Glu Ser Val Ala
5360 5365 5370

gct cca gtg gct gtg tct gcg ccg gtg gct gag tcg gtg ccg gtg ccg 16350
Ala Pro Val Ala Val Ser Ala Pro Val Ala Glu Ser Val Pro Val Pro
5375 5380 5385 5390

gtg ccg gtg ccg gtt cct gtg ccg gtg tcg gct agg tct gag gct ggg 16398
Val Pro Val Pro Val Pro Val Pro Val Ser Ala Arg Ser Glu Ala Gly
5395 5400 5405

ttg cgg gcg cag gcg gag gcg ttg cgt cag tac gtg gca gtc cgg ccg 16446
Leu Arg Ala Gln Ala Glu Ala Leu Arg Gln Tyr Val Ala Val Arg Pro
5410 5415 5420

gac gtt tcg ctt gcc gat gtg ggt gcg ggt ctg gcc tgt ggg cgg gct 16494
Asp Val Ser Leu Ala Asp Val Gly Ala Gly Leu Ala Cys Gly Arg Ala
5425 5430 5435

gtg ctg gag cat cgt gcg gtc gtc ctg gcc gcg gac cgt gag gag ctg 16542
Val Leu Glu His Arg Ala Val Val Leu Ala Ala Asp Arg Glu Glu Leu
5440 5445 5450

gtg caa ggg ttg ggg gcg ctg gcg gcg ggt gag ccg gat cgg cgg gtg 16590
Val Gln Gly Leu Gly Ala Leu Ala Ala Gly Glu Pro Asp Arg Arg Val
5455 5460 5465 5470

acc acg ggt cat gcg ccg ggt ggt gac cgg ggc ggt gtc gtc ttc gtg 16638
Thr Thr Gly His Ala Pro Gly Gly Asp Arg Gly Gly Val Val Phe Val
5475 5480 5485

ttt ccc gga cag ggt ggg cag tgg gcc ggg atg ggt gtg cgt ctg ctc 16686
Phe Pro Gly Gln Gly Gly Gln Trp Ala Gly Met Gly Val Arg Leu Leu
5490 5495 5500

gcc tcc tct ccg gtg ttc gcc cgg cgg atg cag gcg tgc gag gag gct 16734
Ala Ser Ser Pro Val Phe Ala Arg Arg Met Gln Ala Cys Glu Glu Ala
5505 5510 5515

ctg gcg ccg tgg gtg gac tgg tct gtg gtg gac atc ctg cgc cgg gac 16782
Leu Ala Pro Trp Val Asp Trp Ser Val Val Asp Ile Leu Arg Arg Asp
5520 5525 5530

gcg ggg gat gcg gtg tgg gag cgg gcc gat gtg gtc cag cct gtg ctg 16830
Ala Gly Asp Ala Val Trp Glu Arg Ala Asp Val Val Gln Pro Val Leu
5535 5540 5545 5550

ttc agc gtc atg gtg tct ttg gct gct ctg tgg cgt tcc tac ggt atc 16878
Phe Ser Val Met Val Ser Leu Ala Ala Leu Trp Arg Ser Tyr Gly Ile
5555 5560 5565

gaa ccc gac gcg gtc ctt ggc cat tcc cag ggc gag atc gcg gcc gcg 16926
Glu Pro Asp Ala Val Leu Gly His Ser Gln Gly Glu Ile Ala Ala Ala
5570 5575 5580

cat gtg tgt ggg gcg ctg agc ctg aag gac gcg gcg aag act gtt gcg 16974
His Val Cys Gly Ala Leu Ser Leu Lys Asp Ala Ala Lys Thr Val Ala
5585 5590 5595

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ctg cgc agc cgg gcg ctg gcc gct gtg cgg ggc cgg ggc ggc atg gcc   17022
Leu Arg Ser Arg Ala Leu Ala Ala Val Arg Gly Arg Gly Gly Met Ala
   5600                5605                5610

tca gtg ccg ctg cct gcc cag gag gtg gag cag ctc att ggt gag cgg   17070
Ser Val Pro Leu Pro Ala Gln Glu Val Glu Gln Leu Ile Gly Glu Arg
5615                5620                5625                5630

tgg gcg ggg cgg ttg tgg gtg gcg gcg gtc aac ggc ccc cgc tcc acc   17118
Trp Ala Gly Arg Leu Trp Val Ala Ala Val Asn Gly Pro Arg Ser Thr
               5635                5640                5645

gcc gtc tcg ggg gat gcc gag gcg gtg gac gag gtg ctg gcg tac tgt   17166
Ala Val Ser Gly Asp Ala Glu Ala Val Asp Glu Val Leu Ala Tyr Cys
           5650                5655                5660

gcc ggc acc ggg gtg cgg gcc cgg cgg atc ccg gtc gac tat gcc tcg   17214
Ala Gly Thr Gly Val Arg Ala Arg Arg Ile Pro Val Asp Tyr Ala Ser
       5665                5670                5675

cac tgc ccc cat gtg cag ccc ctg cgg gag gag ttg ctg gag ctg ctg   17262
His Cys Pro His Val Gln Pro Leu Arg Glu Glu Leu Leu Glu Leu Leu
   5680                5685                5690

ggg gac atc agc ccg cag ccg tcc ggc gtg ccg ttc ttc tcc acg gtg   17310
Gly Asp Ile Ser Pro Gln Pro Ser Gly Val Pro Phe Phe Ser Thr Val
5695                5700                5705                5710

gag ggc acc tgg ctg gac acc aca acc ctg gac gcc gcc tac tgg tac   17358
Glu Gly Thr Trp Leu Asp Thr Thr Thr Leu Asp Ala Ala Tyr Trp Tyr
               5715                5720                5725

cgc aac ctg cac cag cct gtc cgt ttc agc gat gcc gtc cag gcc ctg   17406
Arg Asn Leu His Gln Pro Val Arg Phe Ser Asp Ala Val Gln Ala Leu
           5730                5735                5740

gcg gat gac gga cac cgc gtc ttc gtc gaa gtc agc ccc cac ccc acc   17454
Ala Asp Asp Gly His Arg Val Phe Val Glu Val Ser Pro His Pro Thr
       5745                5750                5755

ctc gtc ccc gcc atc gaa gac acc acc gaa gac acc gcc gaa gac gtc   17502
Leu Val Pro Ala Ile Glu Asp Thr Thr Glu Asp Thr Ala Glu Asp Val
   5760                5765                5770

acc gcg atc ggc agc ctc cgc cgc ggc gac aac gac acc cgc cgc ttc   17550
Thr Ala Ile Gly Ser Leu Arg Arg Gly Asp Asn Asp Thr Arg Arg Phe
5775                5780                5785                5790

ctc acc gcc ctc gcc cac acc cac acc acc ggc atc ggc aca ccc acc   17598
Leu Thr Ala Leu Ala His Thr His Thr Thr Gly Ile Gly Thr Pro Thr
               5795                5800                5805

acc tgg cac cac cac tac acc cac cac cac acc cac ccc cac aac cac   17646
Thr Trp His His His Tyr Thr His His His Thr His Pro His Asn His
           5810                5815                5820

cac ctc gac ctc ccc act tat ccc ttc caa cgc cag cac tac tgg ctc   17694
His Leu Asp Leu Pro Thr Tyr Pro Phe Gln Arg Gln His Tyr Trp Leu
       5825                5830                5835
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gac gct ccc acg gga gca ggt gac gtc gcc gct gct ggc ttg gag ccg   17742
Asp Ala Pro Thr Gly Ala Gly Asp Val Ala Ala Ala Gly Leu Glu Pro
   5840                5845                5850

gcc gaa cac cct ctg ctc gcg gca aca gtc caa ctc gca gac acg gac   17790
Ala Glu His Pro Leu Leu Ala Ala Thr Val Gln Leu Ala Asp Thr Asp
5855                5860                5865                5870

ggc tgc cta ctg acg ggt cgc ctg tcc ttg cgc tcg cat ccg tgg ctg   17838
Gly Cys Leu Leu Thr Gly Arg Leu Ser Leu Arg Ser His Pro Trp Leu
                5875                5880                5885

ggc gat tac gag gtg ggg ggt gcg gtc ctg ctg tcg ggg tcg gcg ttc   17886
Gly Asp Tyr Glu Val Gly Gly Ala Val Leu Leu Ser Gly Ser Ala Phe
           5890                5895                5900

gtg gag ctg gcg gtc cag gtt ggc gaa cgc gtg ggc tgc acc cga atc   17934
Val Glu Leu Ala Val Gln Val Gly Glu Arg Val Gly Cys Thr Arg Ile
       5905                5910                5915

gag caa ctc act gtg cat gcg ccg ctg gtg gtt cct gtg ggt ggg ggt   17982
Glu Gln Leu Thr Val His Ala Pro Leu Val Val Pro Val Gly Gly Gly
   5920                5925                5930

gtg agt gtg cag gtt ggg gtt gcg gct gcg gat ggg gag ggg cgg cgt   18030
Val Ser Val Gln Val Gly Val Ala Ala Ala Asp Gly Glu Gly Arg Arg
5935                5940                5945                5950

ttg gtg agt gtg tat gcg cgg ggt ggg agt gct tgt ggt ggg ggt ggt   18078
Leu Val Ser Val Tyr Ala Arg Gly Gly Ser Ala Cys Gly Gly Gly Gly
                5955                5960                5965

gcg tcg ggt ggg gtg tgg acg tgt cat gcc tcg ggg gtg ctg gtt gag   18126
Ala Ser Gly Gly Val Trp Thr Cys His Ala Ser Gly Val Leu Val Glu
           5970                5975                5980

gct gct gct ggt ggt ggt gtg gtg gtg gat ggt ctg gcg ggg gtg tgg   18174
Ala Ala Ala Gly Gly Gly Val Val Val Asp Gly Leu Ala Gly Val Trp
       5985                5990                5995

ccg ccg cgg ggt gcg gtg gcg gtg gat gtc gat ggt gtc cgt gac cgt   18222
Pro Pro Arg Gly Ala Val Ala Val Asp Val Asp Gly Val Arg Asp Arg
   6000                6005                6010

ttg gct ggg gct ggt tgt gtt ttg ggg ccg gtg ttt tcg ggg ctg cgt   18270
Leu Ala Gly Ala Gly Cys Val Leu Gly Pro Val Phe Ser Gly Leu Arg
6015                6020                6025                6030

gcg gtg tgg cgt gat ggg ggg gat ttg ctg gct gag gtg tgt ctg ccg   18318
Ala Val Trp Arg Asp Gly Gly Asp Leu Leu Ala Glu Val Cys Leu Pro
                6035                6040                6045

gag gag gcg tgg ggt gat gcg gct ggt ttt ggg ctg cat ccg gcg ttg   18366
Glu Glu Ala Trp Gly Asp Ala Ala Gly Phe Gly Leu His Pro Ala Leu
           6050                6055                6060

ctg gat ggt gtg gtc cag ccg ttg tcg gtg ttg ctt ccg ggt ggg acg   18414
Leu Asp Gly Val Val Gln Pro Leu Ser Val Leu Leu Pro Gly Gly Thr
       6065                6070                6075
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ggg ttt ggg gag ggg gcg ggg ttc ggg gag ggt gtt cgg gtg ccg gct   18462
Gly Phe Gly Glu Gly Ala Gly Phe Gly Glu Gly Val Arg Val Pro Ala
   6080                6085                6090

gtg tgg ggt ggt gtg tcg ctt cac cgg gcg ggt gtg acc ggt gtg cgg   18510
Val Trp Gly Gly Val Ser Leu His Arg Ala Gly Val Thr Gly Val Arg
6095               6100                6105                6110

gtg cgt gtg tgg gct gta ggg cgg ggc ggc ggg cgt gag gcg gtg tcg   18558
Val Arg Val Trp Ala Val Gly Arg Gly Gly Gly Arg Glu Ala Val Ser
               6115                6120                6125

gtc gtg gtc ggg gat gag gcg ggt gtg ccg gtg gcg tcg gtc gat cgt   18606
Val Val Val Gly Asp Glu Ala Gly Val Pro Val Ala Ser Val Asp Arg
           6130                6135                6140

ctt gag ttg cgg cct gtg gat atg ggt cag ttg cgt gct gtc tcg gtt   18654
Leu Glu Leu Arg Pro Val Asp Met Gly Gln Leu Arg Ala Val Ser Val
       6145                6150                6155

tcg gcg ggg cgg cgg ggt tcg ctg tat gcg gtg cag tgg gct gag gtg   18702
Ser Ala Gly Arg Arg Gly Ser Leu Tyr Ala Val Gln Trp Ala Glu Val
   6160                6165                6170

ggt cct gtg ccg gtg tgt ggg cag gcg tgg gcg tgg cac gag gac gtg   18750
Gly Pro Val Pro Val Cys Gly Gln Ala Trp Ala Trp His Glu Asp Val
6175               6180                6185                6190

ggt gag agc ggt ggt ggg cct gtg ccg ggg gtg gtg gtg ttg cgg tgc   18798
Gly Glu Ser Gly Gly Gly Pro Val Pro Gly Val Val Val Leu Arg Cys
               6195                6200                6205

ccg gat gcc ggt gcc ggt ggc ggc ggt ggc ggt ggt gtg ggt gag gtt   18846
Pro Asp Ala Gly Ala Gly Gly Gly Gly Gly Gly Gly Val Gly Glu Val
           6210                6215                6220

gtt ggt ggg gtg ttg ggt gtg gtg cag ggg tgg ctg ggg ctg gag cgg   18894
Val Gly Gly Val Leu Gly Val Val Gln Gly Trp Leu Gly Leu Glu Arg
       6225                6230                6235

ttt gcg ggt tcg cgg ctg gtg gtg gtg acc cgg ggt gcg gtg gtg gcc   18942
Phe Ala Gly Ser Arg Leu Val Val Val Thr Arg Gly Ala Val Val Ala
   6240                6245                6250

ggc caa gaa gac ggc ccg gtg gat gtg gtg ggt gcg gcg gtg tgg ggg   18990
Gly Gln Glu Asp Gly Pro Val Asp Val Val Gly Ala Ala Val Trp Gly
6255               6260                6265                6270

ctg gtg cgg tcg gcg cag gct gag cat ccg gac cgg ttt gtc ctc ctc   19038
Leu Val Arg Ser Ala Gln Ala Glu His Pro Asp Arg Phe Val Leu Leu
               6275                6280                6285

gac ctc gac acc gac acc gac acc ggc acc gac ctc gac acc ggt gct   19086
Asp Leu Asp Thr Asp Thr Asp Thr Gly Thr Asp Leu Asp Thr Gly Ala
           6290                6295                6300

ggt gct ggt gct ggt gct ggt tgg ggc gtg gat ggt ggg cat gtg gcg   19134
Gly Ala Gly Ala Gly Ala Gly Trp Gly Val Asp Gly Gly His Val Ala
       6305                6310                6315
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gcg gtg gtg gcg tgt ggt gag ccg cag ttg gcg gtg cgt ggt gag cgg   19182
Ala Val Val Ala Cys Gly Glu Pro Gln Leu Ala Val Arg Gly Glu Arg
   6320                6325                6330

gtg ctg gcc gca cgc ctg acg cga ctt gag tcg tcc gtt gat gta cct   19230
Val Leu Ala Ala Arg Leu Thr Arg Leu Glu Ser Ser Val Asp Val Pro
6335               6340                6345                6350

gct cag cgg tcc ggt gat gtt gct ggt cgg gag gtg ttg ccg tgg ttg   19278
Ala Gln Arg Ser Gly Asp Val Ala Gly Arg Glu Val Leu Pro Trp Leu
               6355                6360                6365

tcg ggt ggg tcg gtg ttg gtg acg ggt ggg acg ggt gtg ctg ggt gcg   19326
Ser Gly Gly Ser Val Leu Val Thr Gly Gly Thr Gly Val Leu Gly Ala
           6370                6375                6380

gcg gtg gcg cgg cat ctg gct ggt gtg tgt ggg gtg cgg gat ctg ctg   19374
Ala Val Ala Arg His Leu Ala Gly Val Cys Gly Val Arg Asp Leu Leu
       6385                6390                6395

ttg gtg agc cgg cgt ggt ccg gat gct ccg ggt gcg gag ggt ttg cgg   19422
Leu Val Ser Arg Arg Gly Pro Asp Ala Pro Gly Ala Glu Gly Leu Arg
   6400                6405                6410

gcg gag ctg gcc gcg ttg ggg gcg gag gtg cgg att gtt gcg tgt gat   19470
Ala Glu Leu Ala Ala Leu Gly Ala Glu Val Arg Ile Val Ala Cys Asp
6415               6420                6425                6430

gtg ggg gag cgg cgg gag gtg gtc cgg ctg ctg gag ggt gtt cct gcc   19518
Val Gly Glu Arg Arg Glu Val Val Arg Leu Leu Glu Gly Val Pro Ala
               6435                6440                6445

ggg tgt ccg ctg acg ggt gtc gtg cat gcg gct ggt gtg ctg gac gat   19566
Gly Cys Pro Leu Thr Gly Val Val His Ala Ala Gly Val Leu Asp Asp
           6450                6455                6460

gcg acg atc gcc tct ctc acg ccc gag cgg ctg ggc acg gtg ttc gcg   19614
Ala Thr Ile Ala Ser Leu Thr Pro Glu Arg Leu Gly Thr Val Phe Ala
       6465                6470                6475

gcc aag gtg gat gcc gct ctt ttg ctg gat gag ctg acg cgg ggt atg   19662
Ala Lys Val Asp Ala Ala Leu Leu Leu Asp Glu Leu Thr Arg Gly Met
   6480                6485                6490

gag ctg tcg gcg ttc gtg ctg ttc tcc tcg gcc gcg ggg atc ctg ggg   19710
Glu Leu Ser Ala Phe Val Leu Phe Ser Ser Ala Ala Gly Ile Leu Gly
6495               6500                6505                6510

tcg gcc ggg cag ggc aac tac gcc gcg gcc aat gcc gct ctg gac gcg   19758
Ser Ala Gly Gln Gly Asn Tyr Ala Ala Ala Asn Ala Ala Leu Asp Ala
               6515                6520                6525

ctg gcg tac cgg cgg cgg gcg gcg ggt ctg ccg ggg gtg tcg ctg gcg   19806
Leu Ala Tyr Arg Arg Arg Ala Ala Gly Leu Pro Gly Val Ser Leu Ala
           6530                6535                6540

tgg ggg ctg tgg gaa gag gcc agc ggg atg acc ggg cac ctg gcc ggc   19854
Trp Gly Leu Trp Glu Glu Ala Ser Gly Met Thr Gly His Leu Ala Gly
       6545                6550                6555
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acc gac cac cgg cgc atc atc cgt tcc ggt ctg cat ccc atg tcg acc   19902
Thr Asp His Arg Arg Ile Ile Arg Ser Gly Leu His Pro Met Ser Thr
   6560                6565                6570

ccg gac gca ctg gct ctc ttc gat gcg gcc ctg gct ctg gac cgg ccg   19950
Pro Asp Ala Leu Ala Leu Phe Asp Ala Ala Leu Ala Leu Asp Arg Pro
6575               6580                6585                6590

gtc ctg ctg ccc gcc gac ctg cgt ccc gcc ccg ccc ctg ccg ccc ctg   19998
Val Leu Leu Pro Ala Asp Leu Arg Pro Ala Pro Pro Leu Pro Pro Leu
               6595                6600                6605

ctg cag gac ctc ctg ccc gcc acc cgc cgc cgc acc acc cgc acc acc   20046
Leu Gln Asp Leu Leu Pro Ala Thr Arg Arg Arg Thr Thr Arg Thr Thr
           6610                6615                6620

act acc ggt ggt gcg gac aac ggc gcc cag ctg cat gcc cgg ctg gcc   20094
Thr Thr Gly Gly Ala Asp Asn Gly Ala Gln Leu His Ala Arg Leu Ala
       6625                6630                6635

ggc cag aca cac gaa caa cag cac acc acc ctc ctc gcc ctg gtc cgc   20142
Gly Gln Thr His Glu Gln Gln His Thr Thr Leu Leu Ala Leu Val Arg
   6640                6645                6650

tcc cac atc gcc acc gtc ctc ggc cac acc acc ccc gac acc atc ccc   20190
Ser His Ile Ala Thr Val Leu Gly His Thr Thr Pro Asp Thr Ile Pro
6655                6660                6665                6670

ccc gac cgc gcg ttc cgc gac ctc ggc ttc gac tcc ctc acc gcc gtc   20238
Pro Asp Arg Ala Phe Arg Asp Leu Gly Phe Asp Ser Leu Thr Ala Val
               6675                6680                6685

gaa cta cgc aac cgg ctc tcc cgc acc acc gga ctc cgc ctc ccc acc   20286
Glu Leu Arg Asn Arg Leu Ser Arg Thr Thr Gly Leu Arg Leu Pro Thr
           6690                6695                6700

acc ctc gcc ttc gac cac ccc aac ccc acc acc ctc acc cac cac ctc   20334
Thr Leu Ala Phe Asp His Pro Asn Pro Thr Thr Leu Thr His His Leu
       6705                6710                6715

cac aca caa ctt ctg ggc tcg gac agc act gcc tcc atc cca gct ccc   20382
His Thr Gln Leu Leu Gly Ser Asp Ser Thr Ala Ser Ile Pro Ala Pro
   6720                6725                6730

cgt gct gcg gct gtg cct gca gac cag gac gag ccc gtc gcg atc att   20430
Arg Ala Ala Ala Val Pro Ala Asp Gln Asp Glu Pro Val Ala Ile Ile
6735                6740                6745                6750

ggc atg gcg tgc cgc tat ccc gga ggc gtc acc tca gcc gag gag ctg   20478
Gly Met Ala Cys Arg Tyr Pro Gly Gly Val Thr Ser Ala Glu Glu Leu
               6755                6760                6765

tgg gaa ctg ctc gca tcg ggg agg gac acg gtc ggc gag ttt ccg acg   20526
Trp Glu Leu Leu Ala Ser Gly Arg Asp Thr Val Gly Glu Phe Pro Thr
           6770                6775                6780

gac cgt ggg tgg gac ctg gaa gca ctg ttc gat ccg gaa ccg ggt cgg   20574
Asp Arg Gly Trp Asp Leu Glu Ala Leu Phe Asp Pro Glu Pro Gly Arg
       6785                6790                6795
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ccg ggc acc tcg tac acc cgc tgt ggg agt ttc ctc tac gac gcg ggg   20622
Pro Gly Thr Ser Tyr Thr Arg Cys Gly Ser Phe Leu Tyr Asp Ala Gly
   6800                6805                6810

gag ttc gac gcc ggc ttc ttc ggg atc agt ccg cgt gag gca ctg gcg   20670
Glu Phe Asp Ala Gly Phe Phe Gly Ile Ser Pro Arg Glu Ala Leu Ala
6815               6820                6825                6830

atg gac ccg cag cag cga ttg ctg ctg gag gcc tca tgg gag gcc atg   20718
Met Asp Pro Gln Gln Arg Leu Leu Leu Glu Ala Ser Trp Glu Ala Met
               6835                6840                6845

gag cag gca ggt att gac cct acg acc gta cgc ggg agc cag aca ggc   20766
Glu Gln Ala Gly Ile Asp Pro Thr Thr Val Arg Gly Ser Gln Thr Gly
           6850                6855                6860

gtg ttc gcg ggc ctc att ccg cag gcc tat gga ccc agg ctg cac gaa   20814
Val Phe Ala Gly Leu Ile Pro Gln Ala Tyr Gly Pro Arg Leu His Glu
       6865                6870                6875

aac gcc gca gcc gac acc gag ggc tat gtc ctg acc ggc aca tcc ggg   20862
Asn Ala Ala Ala Asp Thr Glu Gly Tyr Val Leu Thr Gly Thr Ser Gly
   6880                6885                6890

agt gtg gcc tcc ggt cgt atc tcg tac acg ttt ggt ttt gag ggt cct   20910
Ser Val Ala Ser Gly Arg Ile Ser Tyr Thr Phe Gly Phe Glu Gly Pro
6895               6900                6905                6910

gcg gtg tcg gtg gac acg gct tgt tcc tcg tcg ttg gtg gct tta cat   20958
Ala Val Ser Val Asp Thr Ala Cys Ser Ser Ser Leu Val Ala Leu His
               6915                6920                6925

ctg gcc tgt cag gcg ttg cgt gcg ggt gag tgc tcg atg gcg ctt gcc   21006
Leu Ala Cys Gln Ala Leu Arg Ala Gly Glu Cys Ser Met Ala Leu Ala
           6930                6935                6940

ggg ggt gtg acg gtg atg tcg tct ccg ggt gcc ttc gtg gag ttt tcg   21054
Gly Gly Val Thr Val Met Ser Ser Pro Gly Ala Phe Val Glu Phe Ser
       6945                6950                6955

cgg cag cgg ggt ctg gcc gcg gac ggg cat tgc aag gcg ttc tcg gcg   21102
Arg Gln Arg Gly Leu Ala Ala Asp Gly His Cys Lys Ala Phe Ser Ala
   6960                6965                6970

gcg gcg gac ggg acc ggc tgg ggt gag ggt gtg ggg atg ctg ctg gtg   21150
Ala Ala Asp Gly Thr Gly Trp Gly Glu Gly Val Gly Met Leu Leu Val
6975               6980                6985                6990

gag cgg ctc tcc gac gcc cgt cgc aac ggt cac cgt gtc ctg gcc gtg   21198
Glu Arg Leu Ser Asp Ala Arg Arg Asn Gly His Arg Val Leu Ala Val
               6995                7000                7005

gtg cgt ggc agt gcg gtc aac cag gac ggt gcg agc aac ggg ctg acc   21246
Val Arg Gly Ser Ala Val Asn Gln Asp Gly Ala Ser Asn Gly Leu Thr
           7010                7015                7020

gcg ccc aac ggg ccc tcc cag cag cgt gtc atc cgc cag gcc ctc gcc   21294
Ala Pro Asn Gly Pro Ser Gln Gln Arg Val Ile Arg Gln Ala Leu Ala
       7025                7030                7035
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gca ggc gaa ccc cac ccc gcc gtc atc cac agc agc gcc cca ggc ggg 22062
Ala Gly Glu Pro His Pro Ala Val Ile His Ser Ser Ala Pro Gly Gly
7280 7285 7290

acc ggg acc ggg gag gcc gca gga aag acc gca ttc atc tgc tcc gga 22110
Thr Gly Thr Gly Glu Ala Ala Gly Lys Thr Ala Phe Ile Cys Ser Gly
7295 7300 7305 7310

cag ggc acc caa cgc ccc ggc atg gcc cac ggc ctc tac cac acc cac 22158
Gln Gly Thr Gln Arg Pro Gly Met Ala His Gly Leu Tyr His Thr His
7315 7320 7325

ccc gtc ttc gcc gcc gca ctc aac gac atc tgc acc cac ctc gac ccc 22206
Pro Val Phe Ala Ala Ala Leu Asn Asp Ile Cys Thr His Leu Asp Pro
7330 7335 7340

cac ctc gac cac ccc ctc ctc ccc ctc ctc acc cag gac ccc aac acc 22254
His Leu Asp His Pro Leu Leu Pro Leu Leu Thr Gln Asp Pro Asn Thr
7345 7350 7355

cag gac acc acc acc ctc gaa gaa gcg gcc gca ctg ctc cag cag acc 22302
Gln Asp Thr Thr Thr Leu Glu Glu Ala Ala Ala Leu Leu Gln Gln Thr
7360 7365 7370

ccg tac gcc cag ccc gcc ctc ttc gcc ttc cag gtc gcc ctc cac cgc 22350
Pro Tyr Ala Gln Pro Ala Leu Phe Ala Phe Gln Val Ala Leu His Arg
7375 7380 7385 7390

ctc ctc acc gac ggc tac cac atc acc ccc cac tac tac gcc gga cac 22398
Leu Leu Thr Asp Gly Tyr His Ile Thr Pro His Tyr Tyr Ala Gly His
7395 7400 7405

tcc ctc ggc gaa atc acc gcc gcc cac ctc gcc ggc atc ctc acc ctc 22446
Ser Leu Gly Glu Ile Thr Ala Ala His Leu Ala Gly Ile Leu Thr Leu
7410 7415 7420

acc gac gcc acc acc ctc atc acc caa cgc gcc acc ctc atg caa acc 22494
Thr Asp Ala Thr Thr Leu Ile Thr Gln Arg Ala Thr Leu Met Gln Thr
7425 7430 7435

atg ccc ccc ggc acc atg acc acc ctc cac acc acc ccc cac cac atc 22542
Met Pro Pro Gly Thr Met Thr Thr Leu His Thr Thr Pro His His Ile
7440 7445 7450

acc cac cac atc acc gcc cac gaa aac gac ctc gcc atc gcc gcc atc 22590
Thr His His Ile Thr Ala His Glu Asn Asp Leu Ala Ile Ala Ala Ile
7455 7460 7465 7470

aac acc ccc acc tcc ctc gtc atc agc ggc acc ccc cac acc gtc caa 22638
Asn Thr Pro Thr Ser Leu Val Ile Ser Gly Thr Pro His Thr Val Gln
7475 7480 7485

cac atc acc acc ctc tgc caa caa caa ggc atc aaa acc aaa acc ctc 22686
His Ile Thr Thr Leu Cys Gln Gln Gln Gly Ile Lys Thr Lys Thr Leu
7490 7495 7500

ccc acc aac cac gcc ttc cac tcc ccc cac acc aac ccc atc ctc aac 22734
Pro Thr Asn His Ala Phe His Ser Pro His Thr Asn Pro Ile Leu Asn
7505 7510 7515

caa ctc cac cag cac acc caa acc ctc acc tac cac cca ccc cac acc 22782
Gln Leu His Gln His Thr Gln Thr Leu Thr Tyr His Pro Pro His Thr
7520 7525 7530

ccc ctc atc acc gcc aac acc cca ccc gac caa ctc ctc acc ccc cac 22830
Pro Leu Ile Thr Ala Asn Thr Pro Pro Asp Gln Leu Leu Thr Pro His
7535 7540 7545 7550

tac tgg acc caa caa gcc cgc aac acc gtc gac ata gcc acc acc acc 22878
Tyr Trp Thr Gln Gln Ala Arg Asn Thr Val Asp Ile Ala Thr Thr Thr
7555 7560 7565

caa acc ctc cac caa cac ggc gtc acc acc tac atc gaa ctc gga ccc 22926
Gln Thr Leu His Gln His Gly Val Thr Thr Tyr Ile Glu Leu Gly Pro
7570 7575 7580

gac aac acc ctc acc acc ctc acc cac cac aac ctc ccc aac acc ccc 22974
Asp Asn Thr Leu Thr Thr Leu Thr His His Asn Leu Pro Asn Thr Pro
7585 7590 7595

acc acc acc ctc acc ctc acc cac ccc cac cac cac ccc caa acc cac 23022
Thr Thr Thr Leu Thr Leu Thr His Pro His His His Pro Gln Thr His
7600 7605 7610

ctc ctc acc aac ctc gcc aaa acc acc acc acc tgg cac ccc cac cac 23070
Leu Leu Thr Asn Leu Ala Lys Thr Thr Thr Thr Trp His Pro His His
7615 7620 7625 7630

tac acc cac cac cac aac caa ccc cac acc cac acc cac ctc gac ctc 23118
Tyr Thr His His His Asn Gln Pro His Thr His Thr His Leu Asp Leu
7635 7640 7645

ccc acc tac ccc ttc caa cac cac cac tac tgg ctc gaa agc aca cag 23166
Pro Thr Tyr Pro Phe Gln His His His Tyr Trp Leu Glu Ser Thr Gln
7650 7655 7660

ccc ggt gcc ggc aac gtg tca gca gcc gga ctc gac ccc acc gaa cac 23214
Pro Gly Ala Gly Asn Val Ser Ala Ala Gly Leu Asp Pro Thr Glu His
7665 7670 7675

ccc cta ctc ggc gcc aca ttg gaa ctg gcc gaa ggg gac ggc tgc cta 23262
Pro Leu Leu Gly Ala Thr Leu Glu Leu Ala Glu Gly Asp Gly Cys Leu
7680 7685 7690

ctg acg ggg cgc ctc tcg ttg cgc acg cat ccc tgg ctc gcc ggc cat 23310
Leu Thr Gly Arg Leu Ser Leu Arg Thr His Pro Trp Leu Ala Gly His
7695 7700 7705 7710

gcg gta ggc ggt gtc gtg ctg ctg ccg ggt acg gcc ttc gcg gaa ctg 23358
Ala Val Gly Gly Val Val Leu Leu Pro Gly Thr Ala Phe Ala Glu Leu
7715 7720 7725

gcc ctt cat gcc gga gaa agt gtg ggt tgc gac cac gtg gac gag ctg 23406
Ala Leu His Ala Gly Glu Ser Val Gly Cys Asp His Val Asp Glu Leu
7730 7735 7740

acg ctc cac aca ccg ttg gtc att cct gag gtc gga gac gtg acc ctt 23454
Thr Leu His Thr Pro Leu Val Ile Pro Glu Val Gly Asp Val Thr Leu
7745 7750 7755

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cag gtt gcc att gcg gcg ccg gac gag tcg ggt cgc cgc atg atg acc   23502
Gln Val Ala Ile Ala Ala Pro Asp Glu Ser Gly Arg Arg Met Met Thr
   7760                7765                7770

atc cac tca cgc ggt gag ggc ggc agt ggt gga gcc gat gcg tcg gcc   23550
Ile His Ser Arg Gly Glu Gly Gly Ser Gly Gly Ala Asp Ala Ser Ala
7775               7780                7785                7790

agt gcg tgg acg cgt cat gcc gcg ggt gtg ctg agc cct gcc aag gac   23598
Ser Ala Trp Thr Arg His Ala Ala Gly Val Leu Ser Pro Ala Lys Asp
               7795                7800                7805

gat gac act gcc tcg tac gag ctg ctt gcg gga ccc tgg cct ccc gtt   23646
Asp Asp Thr Ala Ser Tyr Glu Leu Leu Ala Gly Pro Trp Pro Pro Val
           7810                7815                7820

gga gct acg cct gtc gac ctg aac acg gct tac gat caa atg gcc gac   23694
Gly Ala Thr Pro Val Asp Leu Asn Thr Ala Tyr Asp Gln Met Ala Asp
       7825                7830                7835

gcc ggc ttt gct tat ggc ctg gca ttc caa ggg ttg cgc gcg gcc tgg   23742
Ala Gly Phe Ala Tyr Gly Leu Ala Phe Gln Gly Leu Arg Ala Ala Trp
   7840                7845                7850

cgc tac ggc gac gac atc ctc gtc gag gca cgt ctt ccc gaa gaa gtg   23790
Arg Tyr Gly Asp Asp Ile Leu Val Glu Ala Arg Leu Pro Glu Glu Val
7855               7860                7865                7870

tcg gga gac gcg gcg gcg tac ggt ctg cac ccg gcc ctg ctc gac gct   23838
Ser Gly Asp Ala Ala Ala Tyr Gly Leu His Pro Ala Leu Leu Asp Ala
               7875                7880                7885

gcc ctt cag ggc acc ggc ctg ctt tct gtg gcg ggt ccg ggg acg ccc   23886
Ala Leu Gln Gly Thr Gly Leu Leu Ser Val Ala Gly Pro Gly Thr Pro
           7890                7895                7900

gtc gtg ccc cat gtg tgg aac ggt ctg cgg ttc cgt acg cat ggt gca   23934
Val Val Pro His Val Trp Asn Gly Leu Arg Phe Arg Thr His Gly Ala
       7905                7910                7915

gtc tcc gtg cgc gcg tgc ctg tcg acg ctt gga gcg aca ggg gcg gcc   23982
Val Ser Val Arg Ala Cys Leu Ser Thr Leu Gly Ala Thr Gly Ala Ala
   7920                7925                7930

gtg tgc gtg cgc atc acc gac gac acc ggg gtg ccg gtg gcg tcg gtc   24030
Val Cys Val Arg Ile Thr Asp Asp Thr Gly Val Pro Val Ala Ser Val
7935               7940                7945                7950

gat cgt ctt gag ttg cgg cct gtg gat atg ggt cag ttg cgt gct gtc   24078
Asp Arg Leu Glu Leu Arg Pro Val Asp Met Gly Gln Leu Arg Ala Val
               7955                7960                7965

tcg gtt tcg gcg ggg cgg cgg ggt tcg ctg tat gcg gtg cag tgg gct   24126
Ser Val Ser Ala Gly Arg Arg Gly Ser Leu Tyr Ala Val Gln Trp Ala
           7970                7975                7980

gag gtg ggt cct gtg ccg gtg tgt ggg cag gcg tgg gcg tgg cac gag   24174
Glu Val Gly Pro Val Pro Val Cys Gly Gln Ala Trp Ala Trp His Glu
       7985                7990                7995
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gac gtg ggt gag agc ggt ggt ggg cct gtg ccg ggg gtg gtg gtg ttg   24222
Asp Val Gly Glu Ser Gly Gly Gly Pro Val Pro Gly Val Val Val Leu
   8000                8005                8010

cgg tgc ccg gat gcc ggt gcc gat ggc ggc ggt ggc ggt ggt gtg ggt   24270
Arg Cys Pro Asp Ala Gly Ala Asp Gly Gly Gly Gly Gly Gly Val Gly
8015               8020                8025                8030

gag gtt gtt ggt ggg gtg ttg ggt gtg gtg cag ggg tgg ctg ggg ctg   24318
Glu Val Val Gly Gly Val Leu Gly Val Val Gln Gly Trp Leu Gly Leu
               8035                8040                8045

gag cgg ttt gcg ggt tcg cgg ctg gtg gtg gtg acc cgg ggt gcg gtg   24366
Glu Arg Phe Ala Gly Ser Arg Leu Val Val Val Thr Arg Gly Ala Val
           8050                8055                8060

gtg gcc ggc ccg gag gac ggc ccg gtg gat gtg gtg ggt gcg gcg gtg   24414
Val Ala Gly Pro Glu Asp Gly Pro Val Asp Val Val Gly Ala Ala Val
       8065                8070                8075

tgg ggg ctg gtg cgg tcg gcg cag gct gag cat ccg gac cgg ttt gtc   24462
Trp Gly Leu Val Arg Ser Ala Gln Ala Glu His Pro Asp Arg Phe Val
   8080                8085                8090

ctc ctc gac ctg gac acc gac ctc gac agc ggc gct gac gcc gat gcc   24510
Leu Leu Asp Leu Asp Thr Asp Leu Asp Ser Gly Ala Asp Ala Asp Ala
8095               8100                8105                8110

ggc aac gag gcc ggt atg ggg tct ggt ctg gat ggt ggg cgt gtg gct   24558
Gly Asn Glu Ala Gly Met Gly Ser Gly Leu Asp Gly Gly Arg Val Ala
               8115                8120                8125

gcg gtg gtg gcg tgt ggt gag ccg cag ttg gcg gtg cgt ggt gag cgg   24606
Ala Val Val Ala Cys Gly Glu Pro Gln Leu Ala Val Arg Gly Glu Arg
           8130                8135                8140

gtg ctg gcc gca cgc ctg aca cga ctt gag tcg ccg gtt gat gta tcg   24654
Val Leu Ala Ala Arg Leu Thr Arg Leu Glu Ser Pro Val Asp Val Ser
       8145                8150                8155

ggt cgg gag gtg ttg ccg tgg ttg tcg ggt ggg tcg gtg ttg gtg acg   24702
Gly Arg Glu Val Leu Pro Trp Leu Ser Gly Gly Ser Val Leu Val Thr
   8160                8165                8170

ggt ggg acg ggt gtg ctg ggt gcg gcg gtg gcg cgg cat ctg gct ggt   24750
Gly Gly Thr Gly Val Leu Gly Ala Ala Val Ala Arg His Leu Ala Gly
8175               8180                8185                8190

gtg tgt ggg gtg cgg gat ctg ttg ttg gtg agc cgg cgt ggt ccg gat   24798
Val Cys Gly Val Arg Asp Leu Leu Leu Val Ser Arg Arg Gly Pro Asp
               8195                8200                8205

gct ccg ggt gcg gag ggt ttg cgg gcg gag ctg gcc gcg ttg ggg gcg   24846
Ala Pro Gly Ala Glu Gly Leu Arg Ala Glu Leu Ala Ala Leu Gly Ala
           8210                8215                8220

gag gtg cgg att gtt gcg tgt gat gtg ggg gag cgg cgg gag gtg gtc   24894
Glu Val Arg Ile Val Ala Cys Asp Val Gly Glu Arg Arg Glu Val Val
       8225                8230                8235
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cgg ctg ctg gag ggt gtt cct gcc ggg tgt ccg ctg acg ggt gtc gtg   24942
Arg Leu Leu Glu Gly Val Pro Ala Gly Cys Pro Leu Thr Gly Val Val
   8240                8245                8250

cat gcg gct ggt gtg ctg gac gat gcg acg atc gcc tct ctc acg ccc   24990
His Ala Ala Gly Val Leu Asp Asp Ala Thr Ile Ala Ser Leu Thr Pro
8255               8260                8265                8270

gag cgg ctg ggc acg gtg ttc gcg gcc aag gtg gat gcc gct ctt ttg   25038
Glu Arg Leu Gly Thr Val Phe Ala Ala Lys Val Asp Ala Ala Leu Leu
               8275                8280                8285

ctg gat gag ctg acg cgg ggt atg gag ctg tcg gcg ttc gtg ctg ttc   25086
Leu Asp Glu Leu Thr Arg Gly Met Glu Leu Ser Ala Phe Val Leu Phe
           8290                8295                8300

tcc tcg gcc gcg ggg atc ctg ggg tcg gcc ggg cag ggc aac tac gcc   25134
Ser Ser Ala Ala Gly Ile Leu Gly Ser Ala Gly Gln Gly Asn Tyr Ala
       8305                8310                8315

gcg gcc aat gcc gct ctg gac gcg ctg gcg tac cgg cgg cgg gcg gcg   25182
Ala Ala Asn Ala Ala Leu Asp Ala Leu Ala Tyr Arg Arg Arg Ala Ala
   8320                8325                8330

ggt ctg ccg ggg gtg tcg ctg gcg tgg ggg ctg tgg gaa gag gcc agc   25230
Gly Leu Pro Gly Val Ser Leu Ala Trp Gly Leu Trp Glu Glu Ala Ser
8335               8340                8345                8350

ggg atg acc ggg cac ctg gcc ggc acc gac cac cgg cgc atc atc cgt   25278
Gly Met Thr Gly His Leu Ala Gly Thr Asp His Arg Arg Ile Ile Arg
               8355                8360                8365

tcc ggt ctg cat ccc atg tcg acc ccg gac gca ctg gct ctc ttc gat   25326
Ser Gly Leu His Pro Met Ser Thr Pro Asp Ala Leu Ala Leu Phe Asp
           8370                8375                8380

gcg gcc ctg gct ctg gac cgg ccg gtc ctg ctg ccc gcc gac ctg cgt   25374
Ala Ala Leu Ala Leu Asp Arg Pro Val Leu Leu Pro Ala Asp Leu Arg
       8385                8390                8395

ccc gcc ccg ccc ctg ccg ccc ctg ctg cag gac ctc ctg ccc gcc acc   25422
Pro Ala Pro Pro Leu Pro Pro Leu Leu Gln Asp Leu Leu Pro Ala Thr
   8400                8405                8410

cgc cgc cgc acc acc cgc acc acc act acc ggt ggt gcg gac aac ggc   25470
Arg Arg Arg Thr Thr Arg Thr Thr Thr Thr Gly Gly Ala Asp Asn Gly
8415               8420                8425                8430

gcc cag ctg cat gcc cgg ctg gcc ggc cag aca cac gaa caa cag cac   25518
Ala Gln Leu His Ala Arg Leu Ala Gly Gln Thr His Glu Gln Gln His
               8435                8440                8445

acc acc ctc ctc gcc ctg gtc cgc tcc cac atc gcc acc gtc ctc ggc   25566
Thr Thr Leu Leu Ala Leu Val Arg Ser His Ile Ala Thr Val Leu Gly
           8450                8455                8460

cac aac gcg ccg gag atg atc ccc gtt gac tcg gcg ttc cgc gac cta   25614
His Asn Ala Pro Glu Met Ile Pro Val Asp Ser Ala Phe Arg Asp Leu
       8465                8470                8475
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ggc ttc gac tcc ttg aca gcg gtg gaa ctc cgt aac cgc ctg ggt gag   25662
Gly Phe Asp Ser Leu Thr Ala Val Glu Leu Arg Asn Arg Leu Gly Glu
   8480                8485                8490

gca acg gga ctg cga ctg ccg acc agt ctg gtc ttc gac cag ccg aat   25710
Ala Thr Gly Leu Arg Leu Pro Thr Ser Leu Val Phe Asp Gln Pro Asn
8495               8500                8505                8510

gca gcg acc ctg gcg cgt cac cta cgt cgt gag ctg atg ggc gac gac   25758
Ala Ala Thr Leu Ala Arg His Leu Arg Arg Glu Leu Met Gly Asp Asp
               8515                8520                8525

gcg gaa ggc gag acg cca tcg cag gtc gca ctt cat cag gtt gcc gcg   25806
Ala Glu Gly Glu Thr Pro Ser Gln Val Ala Leu His Gln Val Ala Ala
           8530                8535                8540

gat gag ccg att gcg att gtg ggg atg gcg tgt cgt ttt ccg ggt ggg   25854
Asp Glu Pro Ile Ala Ile Val Gly Met Ala Cys Arg Phe Pro Gly Gly
       8545                8550                8555

gtg tgt tcg ccg gag gag ttg tgg gag ctg gtt gcg tcg ggt ggg gat   25902
Val Cys Ser Pro Glu Glu Leu Trp Glu Leu Val Ala Ser Gly Gly Asp
   8560                8565                8570

gcg att ggt gaa ttt ccg gcc ggt cgg ggg tgg gat ctg gag ggg ttg   25950
Ala Ile Gly Glu Phe Pro Ala Gly Arg Gly Trp Asp Leu Glu Gly Leu
8575               8580                8585                8590

ttt gat tcg gac cct gac cgg tcg ggg acg tcg tac gcg cgg tat ggc   25998
Phe Asp Ser Asp Pro Asp Arg Ser Gly Thr Ser Tyr Ala Arg Tyr Gly
               8595                8600                8605

ggg ttt ttg tat gag gcg ggg gag ttc gat gcg gac ttc ttc ggg atc   26046
Gly Phe Leu Tyr Glu Ala Gly Glu Phe Asp Ala Asp Phe Phe Gly Ile
           8610                8615                8620

agt ccg cgt gag gcg ttg gcg atg gat ccg cag cag cgg ttg ttg ctg   26094
Ser Pro Arg Glu Ala Leu Ala Met Asp Pro Gln Gln Arg Leu Leu Leu
       8625                8630                8635

gag acg tcg tgg gag gcg ttc gag cgg gcg ggt atc gat ccg ctg tcg   26142
Glu Thr Ser Trp Glu Ala Phe Glu Arg Ala Gly Ile Asp Pro Leu Ser
   8640                8645                8650

atg cgt ggc tcc cgt acg ggt gtc ttc gcc ggg gtg atg tac cac gac   26190
Met Arg Gly Ser Arg Thr Gly Val Phe Ala Gly Val Met Tyr His Asp
8655               8660                8665                8670

tac gcc gcg cgt ctc cac cat gtc ccc gag ggt ttc gaa ggc ctc atc   26238
Tyr Ala Ala Arg Leu His His Val Pro Glu Gly Phe Glu Gly Leu Ile
               8675                8680                8685

gcc aac ggc agc gca ggc agc gtc gcg acc ggc cgg gtg gcc tac agc   26286
Ala Asn Gly Ser Ala Gly Ser Val Ala Thr Gly Arg Val Ala Tyr Ser
           8690                8695                8700

ttt ggc ctt gag ggt ccg gcc gtg acc gtc gat acg gcg tgt tcg tcg   26334
Phe Gly Leu Glu Gly Pro Ala Val Thr Val Asp Thr Ala Cys Ser Ser
       8705                8710                8715
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tcg ttg gtg gcg ttg cat tgg gcg gcg cag gcg ttg cgt gcg ggt gag   26382
Ser Leu Val Ala Leu His Trp Ala Ala Gln Ala Leu Arg Ala Gly Glu
   8720                8725                8730

tgt tcg atg gcg ctt gcc ggg ggt gtg acg gtg atg tcg tct ccg ggt   26430
Cys Ser Met Ala Leu Ala Gly Gly Val Thr Val Met Ser Ser Pro Gly
8735               8740                8745                8750

acg ttt gtg gag ttc tca cgt cag cgg ggt ctg gcc gcg gac ggg cgg   26478
Thr Phe Val Glu Phe Ser Arg Gln Arg Gly Leu Ala Ala Asp Gly Arg
               8755                8760                8765

tgc aag gcc tat tcg gcg gct gct gac ggt acc ggc tgg gcc gag ggt   26526
Cys Lys Ala Tyr Ser Ala Ala Ala Asp Gly Thr Gly Trp Ala Glu Gly
           8770                8775                8780

gtg ggg atg ctg ctg gtg gag cgg ctc tcc gac gcc cgt cgc aac ggt   26574
Val Gly Met Leu Leu Val Glu Arg Leu Ser Asp Ala Arg Arg Asn Gly
       8785                8790                8795

cac cgt gtc ctg gcc gtg gtg cgt ggc agt gcg gtc aac cag gac ggt   26622
His Arg Val Leu Ala Val Val Arg Gly Ser Ala Val Asn Gln Asp Gly
   8800                8805                8810

gcg agc aac ggt ctg acc gcg ccc aac ggg ccc tcc cag cag cgt gtc   26670
Ala Ser Asn Gly Leu Thr Ala Pro Asn Gly Pro Ser Gln Gln Arg Val
8815               8820                8825                8830

atc cgt cag gcc ctg gcc aat gcg gga ctg acc ccg gcc gat gtc gac   26718
Ile Arg Gln Ala Leu Ala Asn Ala Gly Leu Thr Pro Ala Asp Val Asp
               8835                8840                8845

gca gtg gag ggc cac ggc acc ggg acc act ctg ggg gac ccg atc gag   26766
Ala Val Glu Gly His Gly Thr Gly Thr Thr Leu Gly Asp Pro Ile Glu
           8850                8855                8860

gcc cag gca ctc ctg gcc gcc tac gga caa cac cgc ccc cac cac cgc   26814
Ala Gln Ala Leu Leu Ala Ala Tyr Gly Gln His Arg Pro His His Arg
       8865                8870                8875

ccc ttg tgg ctg gga tcc ctc aaa tcc aac atc ggg cac gca cag gcc   26862
Pro Leu Trp Leu Gly Ser Leu Lys Ser Asn Ile Gly His Ala Gln Ala
   8880                8885                8890

gcc gcg ggc gtg ggc gga gtc atc aag atg gtg atg gcc ctg cgc aac   26910
Ala Ala Gly Val Gly Gly Val Ile Lys Met Val Met Ala Leu Arg Asn
8895               8900                8905                8910

ggg ctg ctg cca cag acc ctc cac gtg gac gag ccc acc ccc cag gtc   26958
Gly Leu Leu Pro Gln Thr Leu His Val Asp Glu Pro Thr Pro Gln Val
               8915                8920                8925

gac tgg tcc aca ggc gca gta caa ctc ctg aca caa ccg gtg ccc tgg   27006
Asp Trp Ser Thr Gly Ala Val Gln Leu Leu Thr Gln Pro Val Pro Trp
           8930                8935                8940

ccc gcc gac ccg gcc ggc cgg cca cgc cac gcc ggc gtg tca tca ttc   27054
Pro Ala Asp Pro Ala Gly Arg Pro Arg His Ala Gly Val Ser Ser Phe
       8945                8950                8955
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ggc gtc agc ggc acc aac gcc cat gtg att ttg gag gag gcg cct gcg   27102
Gly Val Ser Gly Thr Asn Ala His Val Ile Leu Glu Glu Ala Pro Ala
   8960                8965                8970

gcg gcg ggc ggt gct gcc ggt ggt ggg gtg tcg gtg ggt gct ccg aat   27150
Ala Ala Gly Gly Ala Ala Gly Gly Gly Val Ser Val Gly Ala Pro Asn
8975               8980                8985                8990

cca gcc ctt ccg gtg gct gag tct gag ccg gtg ccg gtg ccg gtg ccg   27198
Pro Ala Leu Pro Val Ala Glu Ser Glu Pro Val Pro Val Pro Val Pro
               8995                9000                9005

gtg tcg gcg agg tct gag gcc ggg ttg cgg gcg cag gca cag gcg ttg   27246
Val Ser Ala Arg Ser Glu Ala Gly Leu Arg Ala Gln Ala Gln Ala Leu
           9010                9015                9020

cgc cag tac gtg gca gcc cgc ccg gac atg tca cct gcc gac atc ggt   27294
Arg Gln Tyr Val Ala Ala Arg Pro Asp Met Ser Pro Ala Asp Ile Gly
       9025                9030                9035

gcg ggt ctg gcc cgc ggc cgg gcc gta ctg gaa cac cgc gcc gtc atc   27342
Ala Gly Leu Ala Arg Gly Arg Ala Val Leu Glu His Arg Ala Val Ile
   9040                9045                9050

ctg gcc gcg gac cgc gag gaa ctg gcg cag gca ctg aca gcc ctg gca   27390
Leu Ala Ala Asp Arg Glu Glu Leu Ala Gln Ala Leu Thr Ala Leu Ala
9055               9060                9065                9070

gcc ggc gaa ccc cac ccc cac atc acc aca ggc cac acc cgg ggc agt   27438
Ala Gly Glu Pro His Pro His Ile Thr Thr Gly His Thr Arg Gly Ser
               9075                9080                9085

gac cgc ggc ggc gtc gtc ttc gtc ttc ccc gga cag ggc ggc cag tgg   27486
Asp Arg Gly Gly Val Val Phe Val Phe Pro Gly Gln Gly Gly Gln Trp
           9090                9095                9100

gcc ggg atg ggc ctg acc ctg ctc acc tcc tca ccc gtg ttc gcc gaa   27534
Ala Gly Met Gly Leu Thr Leu Leu Thr Ser Ser Pro Val Phe Ala Glu
       9105                9110                9115

cac atc gac gca tgc gag aaa gcc ctc acc ccc tgg gtg ccc tgg tcc   27582
His Ile Asp Ala Cys Glu Lys Ala Leu Thr Pro Trp Val Pro Trp Ser
   9120                9125                9130

ctg acc gac atc ctg cac cgc gac ccc gac gac ccc gca tgg caa caa   27630
Leu Thr Asp Ile Leu His Arg Asp Pro Asp Asp Pro Ala Trp Gln Gln
9135               9140                9145                9150

gcc gac gtg gtc cag ccc gtg ctc ttc agc atc atg gtc tcc ctc gcc   27678
Ala Asp Val Val Gln Pro Val Leu Phe Ser Ile Met Val Ser Leu Ala
               9155                9160                9165

gcc ctg tgg cgc tcc tac ggc atc gaa ccc gac gcg gtc ctc ggc cac   27726
Ala Leu Trp Arg Ser Tyr Gly Ile Glu Pro Asp Ala Val Leu Gly His
           9170                9175                9180

tcc cag gga gaa atc gcc gcc gcc cac atc tgc ggc gca ctc agc ctg   27774
Ser Gln Gly Glu Ile Ala Ala Ala His Ile Cys Gly Ala Leu Ser Leu
       9185                9190                9195
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aaa gac gcc gcc aaa acc gtt gca ctg cgc agc cag gca ctg gcc gcc 27822
Lys Asp Ala Ala Lys Thr Val Ala Leu Arg Ser Gln Ala Leu Ala Ala
9200 9205 9210

gta cga ggc cgg ggc gcc atg gtc tca ctg ccc ctg ccc gcc cag gac 27870
Val Arg Gly Arg Gly Ala Met Val Ser Leu Pro Leu Pro Ala Gln Asp
9215 9220 9225 9230

gtg cag cag ctc att tcc gaa cgg tgg gaa ggg cag ttg tgg gtg gca 27918
Val Gln Gln Leu Ile Ser Glu Arg Trp Glu Gly Gln Leu Trp Val Ala
9235 9240 9245

gcc ctc aac ggc ccc cac tcc acc acc gtc tcc ggc gac acc acc gca 27966
Ala Leu Asn Gly Pro His Ser Thr Thr Val Ser Gly Asp Thr Thr Ala
9250 9255 9260

gta gaa gaa ctc ctc acc cac tgt gcc gac acc ggc cta cgg gcc aaa 28014
Val Glu Glu Leu Leu Thr His Cys Ala Asp Thr Gly Leu Arg Ala Lys
9265 9270 9275

cgc atc ccc gtc gac tac gcc tcc cac tgc ccc cac gtc caa ccc ctc 28062
Arg Ile Pro Val Asp Tyr Ala Ser His Cys Pro His Val Gln Pro Leu
9280 9285 9290

cac gac gaa ctc ctg cac ctg ctg gga gac atc acc ccc cag ccg tcc 28110
His Asp Glu Leu Leu His Leu Leu Gly Asp Ile Thr Pro Gln Pro Ser
9295 9300 9305 9310

acc atg ccg ttc ttc tcc acc gtc gta ggg cac ctg gtc tgg tac acc 28158
Thr Met Pro Phe Phe Ser Thr Val Val Gly His Leu Val Trp Tyr Thr
9315 9320 9325

aca acc ctg gac gcc gcc tac tgg tac cgc aac ctc cac cag ccc gtc 28206
Thr Thr Leu Asp Ala Ala Tyr Trp Tyr Arg Asn Leu His Gln Pro Val
9330 9335 9340

cgc ttc agc cac gcc atc cag acc ctg acc gac gac gga cac cgc ccc 28254
Arg Phe Ser His Ala Ile Gln Thr Leu Thr Asp Asp Gly His Arg Pro
9345 9350 9355

ttc atc gaa atc agt ccc cac ccc acc ctc gtc ccc gcc atc gaa gac 28302
Phe Ile Glu Ile Ser Pro His Pro Thr Leu Val Pro Ala Ile Glu Asp
9360 9365 9370

acc acc gaa aac acc acc gaa aac atc acc gcg acc ggc agc ctc cgc 28350
Thr Thr Glu Asn Thr Thr Glu Asn Ile Thr Ala Thr Gly Ser Leu Arg
9375 9380 9385 9390

cgc ggc gac aac gac acc cac cgc ttc ctc acc gcc ctc gcc cac acc 28398
Arg Gly Asp Asn Asp Thr His Arg Phe Leu Thr Ala Leu Ala His Thr
9395 9400 9405

cac acc acc ggc att cgg aca ccc acc acc tgg cac cac cac tac acc 28446
His Thr Thr Gly Ile Arg Thr Pro Thr Thr Trp His His His Tyr Thr
9410 9415 9420

caa acc cac ccc cac ccc cac aac cac cac ctc gac ctg ccc acc tac 28494
Gln Thr His Pro His Pro His Asn His His Leu Asp Leu Pro Thr Tyr
9425 9430 9435

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ccc ttc caa cac cag cac tac tgg ctc caa cca ccc acc acg aca acc   28542
Pro Phe Gln His Gln His Tyr Trp Leu Gln Pro Pro Thr Thr Thr Thr
   9440                9445                9450

gac ctc acc acc acc ggc ctc acc ccc acc cac cac ccc ctc ctc acc   28590
Asp Leu Thr Thr Thr Gly Leu Thr Pro Thr His His Pro Leu Leu Thr
9455               9460                9465                9470

gca aca ctc acc ctc gcc aac aac aac aca caa cta ctc acc ggc cgc   28638
Ala Thr Leu Thr Leu Ala Asn Asn Asn Thr Gln Leu Leu Thr Gly Arg
               9475                9480                9485

ctc tcc cta cgc acc cac ccc tgg ctc acc gac cac acc gtc gtc ggt   28686
Leu Ser Leu Arg Thr His Pro Trp Leu Thr Asp His Thr Val Val Gly
           9490                9495                9500

acc act ctt gtg cca gga acc gcc ctc ctc gaa ctc gcc ctc caa gca   28734
Thr Thr Leu Val Pro Gly Thr Ala Leu Leu Glu Leu Ala Leu Gln Ala
       9505                9510                9515

acc acg acc gac cac ctc gaa gaa ctc gcc ctc cac acg cct ctc gtc   28782
Thr Thr Thr Asp His Leu Glu Glu Leu Ala Leu His Thr Pro Leu Val
   9520                9525                9530

atc ccc cgt gag ggt gcc gtc gac gtt cag gtg cac atc aat cca ccg   28830
Ile Pro Arg Glu Gly Ala Val Asp Val Gln Val His Ile Asn Pro Pro
9535               9540                9545                9550

gac gac acc gac act cgt tca ctg acg atc tac tcg cga agc gag aac   28878
Asp Asp Thr Asp Thr Arg Ser Leu Thr Ile Tyr Ser Arg Ser Glu Asn
               9555                9560                9565

gcc ccc gca gcg gct ccc tgg cgt cat cac gcc acg gcc gtt ctg gga   28926
Ala Pro Ala Ala Ala Pro Trp Arg His His Ala Thr Ala Val Leu Gly
           9570                9575                9580

acc aag acc tcg cgc att gag aca ggc cgt agc cac gat gat ctg tcg   28974
Thr Lys Thr Ser Arg Ile Glu Thr Gly Arg Ser His Asp Asp Leu Ser
       9585                9590                9595

atg tgg ccg cca gcg ggc gca gtt cgc tgt gct gat gag gaa ttg gca   29022
Met Trp Pro Pro Ala Gly Ala Val Arg Cys Ala Asp Glu Glu Leu Ala
   9600                9605                9610

gcc ttg tat ggc gac tac gag gca aat ggc ttt gtc tat ggc ccc gca   29070
Ala Leu Tyr Gly Asp Tyr Glu Ala Asn Gly Phe Val Tyr Gly Pro Ala
9615               9620                9625                9630

ttc cgg ggg ctg act gct gcc tgg cgt ctg gga gac gag gtg ttt gcc   29118
Phe Arg Gly Leu Thr Ala Ala Trp Arg Leu Gly Asp Glu Val Phe Ala
               9635                9640                9645

gag gtt cgc ctt cca gaa cag gtg cac ggc gag gca tcc gcg tac aac   29166
Glu Val Arg Leu Pro Glu Gln Val His Gly Glu Ala Ser Ala Tyr Asn
           9650                9655                9660

ctg cac ccg gca ctg ctg gat gct gcc ttg cac gca gcg gcc ttt gcg   29214
Leu His Pro Ala Leu Leu Asp Ala Ala Leu His Ala Ala Ala Phe Ala
       9665                9670                9675
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ccg tcg ggc agt ctg ccg cag gga tcc gta ccg ttc tcc ttc acc ggt   29262
Pro Ser Gly Ser Leu Pro Gln Gly Ser Val Pro Phe Ser Phe Thr Gly
   9680                9685                9690

gtg acg ctg cac gcc gcc aat gcg tcg tcg ttg cgc gtg cga ctc tcg   29310
Val Thr Leu His Ala Ala Asn Ala Ser Ser Leu Arg Val Arg Leu Ser
9695               9700                9705                9710

ccg gcc gat ccg aac agc ggc cac gcc gca gtt tcc gtg ctg gtc acg   29358
Pro Ala Asp Pro Asn Ser Gly His Ala Ala Val Ser Val Leu Val Thr
               9715                9720                9725

gat gac acc ggt acg ccc gtg gcg tcc gtc gag gcg ttg gcg gtg cgc   29406
Asp Asp Thr Gly Thr Pro Val Ala Ser Val Glu Ala Leu Ala Val Arg
           9730                9735                9740

ccg ttg gcg gcg gac gaa ttg cga gct gcc gag cgc gcc gta cag cgc   29454
Pro Leu Ala Ala Asp Glu Leu Arg Ala Ala Glu Arg Ala Val Gln Arg
       9745                9750                9755

gct gag ctc ttc gac atg aag tgg gtt gag gtg ccc tca gat gta ctg   29502
Ala Glu Leu Phe Asp Met Lys Trp Val Glu Val Pro Ser Asp Val Leu
   9760                9765                9770

gtg tcg ggc ggg gca tcg gtg gtg gtg ctg gat ggt gcc gac gac ctc   29550
Val Ser Gly Gly Ala Ser Val Val Val Leu Asp Gly Ala Asp Asp Leu
9775               9780                9785                9790

gtt ggt ctg gcg gct gag gag gat ggt gtg ccg ggg gtg gtg gtg ttg   29598
Val Gly Leu Ala Ala Glu Glu Asp Gly Val Pro Gly Val Val Val Leu
               9795                9800                9805

cgg tgc ccg gat gcc ggt gcc gat ggc ggc ggt ggt ggc ggt ggt gtg   29646
Arg Cys Pro Asp Ala Gly Ala Asp Gly Gly Gly Gly Gly Gly Gly Val
           9810                9815                9820

ggt gag gtt gtt ggt ggg gtg ttg ggt gtg gtg cag ggg tgg ctg ggg   29694
Gly Glu Val Val Gly Gly Val Leu Gly Val Val Gln Gly Trp Leu Gly
       9825                9830                9835

ctg gag cgg ttt gcg ggt tcg cgg ctg gtg gtg gtg acc cgg ggt gcg   29742
Leu Glu Arg Phe Ala Gly Ser Arg Leu Val Val Val Thr Arg Gly Ala
   9840                9845                9850

gtg gtg gcc ggc ccg gag gac ggc ccg gtg gat ggc ccg gtg gat gtg   29790
Val Val Ala Gly Pro Glu Asp Gly Pro Val Asp Gly Pro Val Asp Val
9855               9860                9865                9870

gtg ggt gcg gcg gtg tgg ggg ctg gtg cgg tcg gcg cag gct gag cat   29838
Val Gly Ala Ala Val Trp Gly Leu Val Arg Ser Ala Gln Ala Glu His
               9875                9880                9885

ccg gac cgg ttt gtc ctc ctc gac ctg gac acc gac ctc gac agc ggc   29886
Pro Asp Arg Phe Val Leu Leu Asp Leu Asp Thr Asp Leu Asp Ser Gly
           9890                9895                9900

gct gac cgc gat gcc ggc aac gag gcc ggt atg ggg tct ggt ctg gat   29934
Ala Asp Arg Asp Ala Gly Asn Glu Ala Gly Met Gly Ser Gly Leu Asp
       9905                9910                9915
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ggt ggg cgt gtg gct gcg gtg gtg gcg tgt ggt gag ccg cag ttg gcg   29982
Gly Gly Arg Val Ala Ala Val Val Ala Cys Gly Glu Pro Gln Leu Ala
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gtg cgt ggt gag cgg gtg ctg gcc gca cgc ctg aca cga ctt gag tcg   30030
Val Arg Gly Glu Arg Val Leu Ala Ala Arg Leu Thr Arg Leu Glu Ser
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ccg gtt gat gta tcg ggt cgg gag gtg ttg ccg tgg ttg tcg ggt ggg   30078
Pro Val Asp Val Ser Gly Arg Glu Val Leu Pro Trp Leu Ser Gly Gly
               9955                9960                9965

tcg gtg ttg gtg acg ggt ggg acg ggt gtg ctg ggt gcg gcg gtg gcg   30126
Ser Val Leu Val Thr Gly Gly Thr Gly Val Leu Gly Ala Ala Val Ala
           9970                9975                9980

cgg cat ctg gct ggt gtg tgt ggg gtg cgg gat ctg ttg ttg gtg agc   30174
Arg His Leu Ala Gly Val Cys Gly Val Arg Asp Leu Leu Leu Val Ser
       9985                9990                9995

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Arg Arg Gly Pro Asp Ala Pro Gly Ala Glu Gly Leu Arg Ala Glu Leu
  10000               10005               10010

gcc gcg ttg ggg gcg gag gtg cgg att gtt gcg tgt gat gtg ggg gag   30270
Ala Ala Leu Gly Ala Glu Val Arg Ile Val Ala Cys Asp Val Gly Glu
10015               10020               10025               10030

cgg cgg gag gtg gtc cgg ctg ctg gag ggt gtt cct gcc ggg tgt ccg   30318
Arg Arg Glu Val Val Arg Leu Leu Glu Gly Val Pro Ala Gly Cys Pro
               10035               10040               10045

ctg acg ggt gtc gtg cat gcg gct ggt gtg ctg gac gat gcg acg atc   30366
Leu Thr Gly Val Val His Ala Ala Gly Val Leu Asp Asp Ala Thr Ile
           10050               10055               10060

gcc tct ctc acg ccc gag cgg ctg ggc acg gtg ttc gcg gcc aag gtg   30414
Ala Ser Leu Thr Pro Glu Arg Leu Gly Thr Val Phe Ala Ala Lys Val
       10065               10070               10075

gat gcc gct ctt ttg ctg gat gag ctg acg cgg ggt atg gag ctg tcg   30462
Asp Ala Ala Leu Leu Leu Asp Glu Leu Thr Arg Gly Met Glu Leu Ser
  10080               10085               10090

gcg ttc gtg ctg ttc tcc tcg gcc gcg ggg atc ctg ggg tcg gcc ggg   30510
Ala Phe Val Leu Phe Ser Ser Ala Ala Gly Ile Leu Gly Ser Ala Gly
10095               10100               10105               10110

cag ggc aac tac gcc gcg gcc aat gcc gct ctg gac gcg ctg gcg tac   30558
Gln Gly Asn Tyr Ala Ala Ala Asn Ala Ala Leu Asp Ala Leu Ala Tyr
               10115               10120               10125

cgg cgg cgg gcg gcg ggt ctg ccg ggg gtg tcg ctg gcg tgg ggg ctg   30606
Arg Arg Arg Ala Ala Gly Leu Pro Gly Val Ser Leu Ala Trp Gly Leu
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tgg gaa gag gcc agc ggg atg acc ggg cat ctg gcc ggc acc gac cac   30654
Trp Glu Glu Ala Ser Gly Met Thr Gly His Leu Ala Gly Thr Asp His
       10145               10150               10155
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Leu Ala Leu Phe Asp Ala Ala Leu Ala Leu Asp Arg Pro Val Leu Leu
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Gly Ala Asp Asn Gly Ala Gln Leu His Gly Arg Leu Ala Gly Gln Thr
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His Glu Gln Gln His Thr Thr Leu Leu Ala Leu Val Arg Ser His Ile
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Ala Thr Val Leu Gly His Thr Thr Pro Asp Thr Ile Pro Pro Asp Arg
10255 10260 10265 10270

gcg ttc cgc gac ctc ggc ttc gac tcc ctc acc gcc gtc gaa cta cgc 31038
Ala Phe Arg Asp Leu Gly Phe Asp Ser Leu Thr Ala Val Glu Leu Arg
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aac cgg ctc tcc cac acc acc gga ctc cgc ctc ccc acc acc ctc gcc 31086
Asn Arg Leu Ser His Thr Thr Gly Leu Arg Leu Pro Thr Thr Leu Ala
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ttc gac cac ccc aac ccc acc acc ctc acc cac cac ctc cac aca caa 31134
Phe Asp His Pro Asn Pro Thr Thr Leu Thr His His Leu His Thr Gln
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ctc gtc agc aag gga ctc acc gcc gcg gcc gag ccg gac gcc gca acg 31182
Leu Val Ser Lys Gly Leu Thr Ala Ala Ala Glu Pro Asp Ala Ala Thr
10320 10325 10330

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Thr Pro Pro Gly Leu Pro Ser Leu Leu Ser Glu Leu Glu Arg Leu Glu
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10385 10390 10395

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gag atg ttc gct ctc atc gac agg gaa gtc gga ttc gaa tct caa tga   31422
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<213> Streptomyces avermitilis

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Pro Gly Gln Gly Pro Gln Trp Pro Gly Met Gly Arg Glu Leu Leu Asp
         35                  40                  45

Ala Ser Asp Val Phe Arg Glu Ser Val Arg Ala Cys Glu Ala Ala Phe
     50                  55                  60

Ala Pro Tyr Val Asp Trp Ser Val Glu Gln Val Leu Arg Asp Ser Pro
 65                  70                  75                  80

Asp Ala Pro Gly Leu Asp Arg Val Asp Val Val Gln Pro Thr Leu Phe
                 85                  90                  95

Ala Val Met Ile Ser Leu Ala Ala Leu Trp Arg Ser Gln Gly Val Glu
            100                 105                 110

Pro Cys Ala Val Leu Gly His Ser Leu Gly Glu Ile Ala Ala Ala His
        115                 120                 125

Val Ser Gly Gly Leu Ser Leu Ala Asp Ala Ala Arg Val Val Thr Leu
    130                 135                 140

Trp Ser Gln Ala Gln Thr Thr Leu Ala Gly Thr Gly Ala Leu Val Ser
145                 150                 155                 160

Val Ala Ala Thr Pro Asp Glu Leu Leu Pro Arg Ile Ala Pro Trp Thr
                165                 170                 175

Glu Asp Asn Pro Ala Arg Leu Ala Val Ala Ala Val Asn Gly Pro Arg
            180                 185                 190

Ser Thr Val Val Ser Gly Ala Arg Glu Ala Val Ala Asp Leu Val Ala
        195                 200                 205

Asp Leu Thr Ala Ala Gln Val Arg Thr Arg Met Ile Pro Val Asp Val
    210                 215                 220

Pro Ala His Ser Pro Leu Met Tyr Ala Ile Glu Glu Arg Val Val Ser
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Gly Leu Leu Pro Ile Thr Pro Arg Pro Ser Arg Ile Pro Phe His Ser
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Ser Val Thr Gly Gly Arg Leu Asp Thr Arg Glu Leu Asp Ala Ala Tyr
            260                 265                 270
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Trp Tyr Arg Asn Met Ser Ser Thr Val Arg Phe Glu Pro Ala Ala Arg
275 280 285

Leu Leu Leu Gln Gln Gly Pro Lys Thr Phe Val Glu Met Ser Pro His
290 295 300

Pro Val Leu Thr Met Gly Leu Gln Glu Leu Ala Pro Asp Leu Gly Asp
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Thr Thr Gly Thr Ala Asp Thr Val Ile Met Gly Thr Leu Arg Arg Gly
325 330 335

Gln Gly Thr Leu Asp His Phe Leu Thr Ser Leu Ala Gln Leu Arg Gly
340 345 350

His Gly Glu Thr Ser Ala Thr Thr Val Leu Ser Ala Arg Leu Thr Ala
355 360 365

Leu Ser Pro Thr Gln Gln Gln Ser Leu Leu Leu Asp Leu Val Arg Ala
370 375 380

His Thr Met Ala Val Leu Asn Asp Asp Gly Asn Glu Arg Thr Ala Ser
385 390 395 400

Asp Ala Gly Pro Ser Ala Ser Phe Ala His Leu Gly Phe Asp Ser Val
405 410 415

Met Gly Val Glu Leu Arg Asn Arg Leu Ser Lys Ala Thr Gly Leu Arg
420 425 430

Leu Pro Val Thr Leu Ile Phe Asp His Thr Thr Pro Ala Ala Val Ala
435 440 445

Ala Arg Leu Arg Thr Ala Ala Leu Gly His Leu Asp Glu Asp Thr Ala
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Pro Val Pro Asp Ser Pro Ser Gly His Gly Gly Thr Ala Ala Ala Asp
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Asp Pro Ile Ala Ile Ile Gly Met Ala Cys Arg Phe Pro Gly Gly Val
485 490 495

Arg Ser Pro Lys Asp Leu Trp Glu Leu Ala Ala Ser Gly Gly Asp Ala
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Ile Gly Pro Phe Pro Thr Asp Arg Gly Trp Pro Thr Glu Gln Arg His
515 520 525

Ala Gln Asp Pro Thr Gln Pro Gly Thr Phe Tyr Pro Gln Gly Gly Gly
530 535 540

Phe Leu His Asp Ala Ala His Phe Asp Ala Gly Phe Phe Gly Ile Ser
545 550 555 560

Pro Arg Glu Ala Leu Ala Met Asp Pro Gln Gln Arg Leu Leu Leu Glu
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Thr Ser Trp Glu Ala Phe Glu Arg Ala Gly Ile Asp Pro Leu Ser Val
580 585 590

Arg Gly Ser Arg Thr Gly Val Phe Ala Gly Ala Leu Ser Phe Asp Tyr
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610 615 620

Gly His Ile Leu Thr Gly Thr Thr Gly Ser Val Leu Ser Gly Arg Ile
625 630 635 640

Ala Tyr Ser Phe Gly Leu Glu Gly Pro Ala Ile Thr Val Asp Thr Gly
645 650 655

Cys Ser Ala Ser Leu Val Thr Leu His Leu Ala Cys Gln Ser Leu Arg
660 665 670

Ser Gly Glu Cys Thr Leu Ala Leu Ala Gly Gly Val Ser Val Met Ser
675 680 685

Thr Leu Gly Met Phe Ile Glu Phe Ser Arg Gln Arg Gly Leu Ser Val
690 695 700

Asp Gly Arg Cys Lys Ala Tyr Ser Ala Ala Ala Asp Gly Thr Gly Trp
705 710 715 720

Gly Glu Gly Val Gly Met Leu Leu Val Glu Arg Leu Ser Asp Ala Val
725 730 735

Arg Leu Gly His Arg Val Leu Ala Val Val Arg Gly Ser Ala Val Asn
740 745 750

Gln Asp Gly Ala Ser Asn Gly Leu Thr Ala Pro Asn Gly Pro Ala Gln
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Pro Trp Pro Gly Asp Ala Ala Gly Arg Leu Arg Arg Ala Gly Val Ser
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Ser Phe Gly Ile Gly Gly Thr Asn Ala His Val Ile Leu Glu Glu Ala
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Pro Ala Ala Gly Gly Cys Val Ala Gly Gly Gly Val Leu Glu Gly Ala
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Pro Gly Leu Ala Ile Ser Val Ala Glu Ser Val Ala Ala Pro Val Ala
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1075 1080 1085

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1090 1095 1100

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His Tyr Thr His His His Thr His Pro His Pro His Thr His Leu Asp
1380 1385 1390

Leu Pro Thr Tyr Pro Phe Gln His Gln His Tyr Trp Leu Glu Ser Ser
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Gln Pro Gly Ala Gly Ser Gly Ser Gly Ala Gly Ala Gly Ser Gly Ala
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Gly Ser Gly Arg Ala Gly Thr Ala Gly Gly Thr Ala Glu Val Glu Ser
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Thr Leu Ala Val Pro Pro Ser Ala Gly Leu Asp Thr Val Val Pro Ala
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Leu Ser Ala Trp His Arg His Gln His Asp Gln Ala Arg Ile Asn Thr
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Trp Thr Tyr Gln Glu Thr Trp Lys Pro Leu Thr Leu Pro Thr Thr His
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Thr Pro Ile Pro Leu Thr Leu Asn His Thr His Thr Asn Pro Gln His
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Leu His His Thr Leu His His Thr Arg Gln Gln Ala Gln Asn His Thr
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Thr Gly Ala Ile Thr Gly Leu Leu Ser Leu Leu Ala Leu Asp Glu Thr
1570 1575 1580

Pro His Pro His His Pro His Thr Pro Thr Gly Thr Leu Leu Asn Leu
1585 1590 1595 1600

Thr Leu Thr Gln Thr His Thr Gln Thr His Pro Pro Thr Pro Leu Trp
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Tyr Ala Thr Thr Asn Ala Thr Thr Thr His Pro Asn Asp Pro Leu Thr
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His Pro Thr Gln Ala Gln Thr Trp Gly Leu Ala Arg Thr Thr Leu Leu
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Glu His Pro Thr His Thr Ala Gly Ile Ile Asp Leu Pro Thr Thr Pro
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Thr Pro His Thr Leu Gln His Leu Thr Gln Thr Leu Thr Gln Pro His
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His Gln Thr Gln Leu Ala Ile Arg Thr Thr Gly Thr His Thr Arg Arg
1685 1690 1695

Leu Thr Pro Thr Thr Leu Thr Pro Thr His Gln Pro Pro Thr Pro Thr
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Pro His Gly Thr Thr Leu Ile Thr Gly Gly Thr Gly Ala Leu Ala Thr
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His Leu Thr His His Leu Thr Thr His Gln Pro Thr Gln His Leu Leu
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1825 1830 1835 1840

Pro Leu Thr Ala Phe Val Leu Tyr Ser Ser Ala Ala Ala Thr Phe Gly
1845 1850 1855

Ala Pro Gly Gln Ala Asn Tyr Ala Ala Ala Asn Ala Tyr Leu Asp Ala
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1875 1880 1885

Trp Gly Thr Trp Gln Gly Asn Gly Leu Ala Asp Ser Asp Lys Ala Arg
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1905 1910 1915 1920

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Val Ile Ala Asp Ile Asp Trp Ser Lys Ile Glu His Thr Ser Gln Thr
1940 1945 1950

Ser Asp Leu Val Ser Ala Ala Arg Glu Arg Glu Pro Ala Val Gln Arg
1955 1960 1965

Pro Thr Pro Pro Ala Glu Leu His Lys Thr Leu Ala His Gln Thr Ser
1970 1975 1980

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1985 1990 1995 2000

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2005 2010 2015

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2225 2230 2235 2240

Ile Ser Tyr Thr Phe Gly Phe Glu Gly Pro Ala Val Ser Val Asp Thr
2245 2250 2255

Ala Cys Ser Ser Ser Leu Val Ala Leu His Leu Ala Cys Gln Ala Leu
2260 2265 2270

Arg Ala Gly Glu Cys Ser Met Ala Leu Ala Gly Gly Val Thr Val Met
2275 2280 2285

Ser Ser Pro Gly Ala Phe Val Glu Phe Ser Arg Gln Arg Gly Leu Ala
2290 2295 2300

Ala Asp Gly His Cys Lys Ala Phe Ser Ala Ala Ala Asp Gly Thr Gly
2305 2310 2315 2320

Trp Gly Glu Gly Val Gly Met Leu Leu Val Glu Arg Leu Ser Asp Ala
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His Arg Asn Gly His Arg Val Leu Ala Val Val Arg Gly Ser Ala Val
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Asn Gln Asp Gly Ala Ser Asn Gly Leu Thr Ala Pro Asn Gly Pro Ser
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Gln Gln Arg Val Ile Arg Gln Ala Leu Ala Asn Ala Gly Leu Ser Ala
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Gly Asp Val Asp Ala Val Glu Ala His Gly Thr Gly Thr Thr Leu Gly
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Asp Pro Ile Glu Ala Gln Ala Leu Leu Ala Thr Tyr Gly Gln Asp Arg
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His Thr Gln Ala Ala Ala Gly Val Ala Gly Val Ile Lys Met Val Met
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Ala Leu Arg His Gly Leu Leu Pro Arg Thr Leu His Val Asp Glu Pro
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Ser Pro His Val Asp Trp Ser Ala Gly Ala Val Gln Leu Leu Thr Glu
2465 2470 2475 2480

Thr Val Pro Trp Pro Gly Gly Glu Gly Arg Leu Arg Arg Ala Gly Val
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Ser Ser Phe Gly Val Ser Gly Thr Asn Ala His Val Ile Leu Glu Glu
2500 2505 2510

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Ala Pro Ala Asp Asp Val Pro Gly Gly Pro Pro Ala Gly Glu Gly Asp
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Ala Gly Ser Asp Asp Glu Ala Ala Ala Gly Ser Pro Gly Val Trp Pro
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Gln His Thr Gln Thr Leu Thr Tyr His Pro Pro His Thr Pro Leu Ile
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<213> Streptomyces avermitilis

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Gly Gly Ala Thr Ser Pro Thr Arg Leu Trp His Leu Val Lys Ser Gln
50 55 60

Thr Asp Ala Ile Gly Glu Phe Pro Thr Asp Arg Gly Trp Asn Leu Glu
65 70 75 80

Gln Leu Tyr Asp Pro Asp Pro Asp Arg Ser Gly Thr Ser Tyr Thr Arg
85 90 95

Ser Gly Gly Phe Leu Tyr Asp Ala Gly Asp Phe Asp Ala Ala Phe Phe
100 105 110

Glu Leu Ser Pro Arg Glu Ala Leu Ala Met Asp Pro Gln Gln Arg Leu
115 120 125

Leu Leu Glu Thr Thr Trp Glu Thr Phe Glu Gln Gly Gly Ile Asp Pro
130 135 140

Arg Ser Met Arg Gly Ser Arg Thr Gly Val Phe Val Gly Ile Asn Pro
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Glu Asp Tyr Thr Thr Gly Tyr Thr His Gln Pro Ser Asn Ala Val Glu
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Cys Ser Ser Ser Leu Val Ala Leu His Leu Ala Cys Gln Ala Leu Arg
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Ser Gly Glu Cys Thr Met Ala Leu Ala Gly Gly Ala Ser Val Met Ala
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Thr Pro Phe Val Phe Thr Glu Phe Ser Arg Gln Arg Gly Leu Ala Ala
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Asp Gly Arg Cys Lys Ala Phe Ser Ala Ala Ala Asp Gly Thr Gly Trp
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Ser Glu Gly Val Gly Met Leu Leu Val Glu Arg Leu Ser Asp Ala Arg
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Gln Asp Gly Ala Ser Asn Gly Leu Thr Ala Pro Asn Gly Arg Ser Gln
305 310 315 320

Val Lys Val Ile Arg Gln Ala Leu Ala Asn Ala His Leu Ser Pro Ala
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Pro Ile Glu Ala Gln Ala Leu Val Glu Ala Tyr Gly Gln Asp Arg Pro
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Pro His Val Asp Trp Ser Ala Gly Ala Val Gln Leu Leu Thr Glu Thr
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Glu Asn Asp Leu Ala Ile Ala Ala Ile Asn Thr Pro Thr Ser Leu Val
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Pro His Thr His Thr His Leu Asp Leu Pro Thr Tyr Pro Phe Gln His
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His His Tyr Trp Leu Gln Pro Pro Gly Lys Pro Ser Asp Pro Ser Pro
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Ser Glu Gly Arg Glu Gln Ala Thr Thr Pro Ser Thr Pro Leu Arg Asp
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Val Leu Val Gly Lys Ser Pro Gln Glu Arg Asp Glu Glu Leu Leu Arg
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Arg Gly Ser Ala Val Asn Gln Asp Gly Ala Ser Asn Gly Leu Thr Ala
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Pro Asn Gly Pro Ser Gln Glu Arg Val Ile Arg Leu Ala Leu Ala Asn
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Gly Thr Thr Leu Gly Asp Pro Ile Glu Ala Gln Ala Leu Leu Ala Thr
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1475 1480 1485

Arg Arg Ala Gly Val Ser Ser Phe Gly Val Ser Gly Thr Asn Ala His
1490 1495 1500

Val Ile Leu Glu Glu Ala Pro Ala His Asn Ile Pro Ser Asp Thr Pro
1505 1510 1515 1520

Ala Asp Asp Ala Pro Gly Glu Ala Ala Ala Asp Asp Val Pro Gly Glu
1525 1530 1535

Ala Ala Gly Asp Asp Ala Gly Thr Gly Gly Glu Ala Thr Gly Pro Ala
1540 1545 1550

Ala Gly Ser Pro Gly Val Trp Pro Trp Leu Val Ser Ala Lys Ser Gln
1555 1560 1565

Pro Ala Leu Arg Ala Gln Ala Gln Ala Leu His Ala His Leu Thr Asp
1570 1575 1580

His Pro Gly Leu Asp Leu Ala Asp Val Gly Tyr Thr Leu Ala His Ala
1585 1590 1595 1600

Arg Ala Val Phe Asp His Arg Ala Thr Leu Ile Ala Ala Asp Arg Asp
1605 1610 1615

Thr Phe Leu Gln Ala Leu Gln Ala Leu Ala Ala Gly Glu Pro His Pro
1620 1625 1630

Ala Val Ile His Ser Ser Ala Pro Gly Gly Thr Gly Thr Gly Glu Ala
1635 1640 1645

Ala Gly Lys Thr Ala Phe Ile Cys Ser Gly Gln Gly Thr Gln Arg Pro
1650 1655 1660

Gly Met Ala His Gly Leu Tyr His Thr His Pro Val Phe Ala Ala Ala
1665 1670 1675 1680

Leu Asn Asp Ile Cys Thr His Leu Asp Pro His Leu Asp His Pro Leu
1685 1690 1695

Leu Pro Leu Leu Thr Gln Asp Pro Asn Thr Gln Asp Thr Thr Thr Leu
1700 1705 1710

Glu Glu Ala Ala Ala Leu Leu Gln Gln Thr Pro Tyr Ala Gln Pro Ala
1715 1720 1725

Leu Phe Ala Phe Gln Val Ala Leu His Arg Leu Leu Thr Asp Gly Tyr
1730 1735 1740

His Ile Thr Pro His Tyr Tyr Ala Gly His Ser Leu Gly Glu Ile Thr
1745 1750 1755 1760

Ala Ala His Leu Ala Gly Ile Leu Thr Leu Thr Asp Ala Thr Thr Leu
1765 1770 1775

Ile Thr Gln Arg Ala Thr Leu Met Gln Thr Met Pro Pro Gly Thr Met
1780 1785 1790

Thr Thr Leu His Thr Thr Pro His His Ile Thr His His Leu Thr Ala
1795 1800 1805

His Glu Asn Asp Leu Ala Ile Ala Ala Ile Asn Thr Pro Thr Ser Leu
1810 1815 1820

Val Ile Ser Gly Thr Pro His Thr Val Gln His Ile Thr Thr Leu Cys
1825 1830 1835 1840

Gln Gln Gln Gly Ile Lys Thr Lys Thr Leu Pro Thr Lys Asn Ala Phe
1845 1850 1855

His Ser Pro His Thr Asn Pro Ile Leu Asn Gln Leu His Gln His Thr
1860 1865 1870

Gln Thr Leu Thr Tyr His Pro Pro His Thr Pro Leu Ile Thr Ala Asn
1875 1880 1885

Thr Pro Pro Asp Gln Leu Leu Thr Pro His Tyr Trp Thr Gln Gln Ala
1890 1895 1900

Arg Asn Thr Val Asp Tyr Ala Thr Thr Thr Gln Thr Leu His Gln His
1905 1910 1915 1920

Gly Val Thr Thr Tyr Ile Glu Leu Gly Pro Asp Asn Thr Leu Thr Thr
1925 1930 1935

Leu Thr His His Asn Leu Pro Asn Thr Pro Thr Thr Thr Leu Thr Leu
1940 1945 1950

Thr His Pro His His His Pro Gln Thr His Leu Leu Thr Asn Leu Ala
1955 1960 1965

Lys Thr Thr Thr Thr Trp His Pro His His Tyr Thr His His His Asn
1970 1975 1980

Gln Pro His Thr His Thr His Leu Asp Leu Pro Thr Tyr Pro Phe Gln
1985 1990 1995 2000

His Gln His Tyr Trp Leu Glu Ser Thr Gln Pro Gly Ala Gly Ser Gly
2005 2010 2015

Ser Gly Ser Gly Ser Gly Arg Ala Gly Thr Ala Gly Gly Thr Ala Glu
2020 2025 2030

Val Glu Ser Arg Phe Trp Asp Ala Val Ala Arg Gln Asp Leu Glu Thr
2035 2040 2045

Val Ala Thr Thr Leu Ala Val Pro Pro Ser Ala Gly Leu Asp Thr Val
2050 2055 2060

Val Pro Ala Leu Ser Ala Trp His Arg His Gln His Asp Gln Ala Arg
2065 2070 2075 2080

Ile Asn Thr Trp Thr Tyr Gln Glu Thr Trp Lys Pro Leu Thr Leu Pro
2085 2090 2095

Thr Thr His Gln Pro His Gln Thr Trp Leu Ile Ala Ile Pro Glu Thr
2100 2105 2110

Gln Thr His His Pro His Ile Thr Asn Ile Leu Thr Asn Leu His His
2115 2120 2125

His Gly Ile Thr Pro Ile Pro Leu Thr Leu Asn His Thr His Thr Asn
2130 2135 2140

Pro Gln His Leu His His Thr Arg Gln Gln Ala Gln Asn His Thr Thr
2145 2150 2155 2160

Gly Pro Ile Thr Gly Leu Leu Ser Leu Leu Ala Leu Asp Glu Thr Pro
2165 2170 2175

His Pro His His Pro His Thr Pro Thr Gly Thr Leu Leu Asn Leu Thr
2180 2185 2190

Leu Thr Gln Thr His Thr Gln Thr His Pro Pro Thr Pro Leu Trp Tyr
2195 2200 2205

Ala Thr Thr Asn Ala Thr Thr Thr His Pro Asn Asp Pro Leu Thr His
2210 2215 2220

Pro Thr Gln Ala Gln Thr Trp Gly Leu Ala Arg Thr Thr Leu Leu Glu
2225 2230 2235 2240

His Pro Thr His Thr Ala Gly Ile Ile Asp Leu Pro Thr Thr Pro Thr
2245 2250 2255

Pro His Thr Leu His His Leu Thr Gln Thr Leu Thr Gln Pro His His
2260 2265 2270

Gln Thr Gln Leu Ala Ile Arg Thr Thr Gly Thr His Thr Arg Arg Leu
2275 2280 2285

Thr Pro Thr Thr Leu Thr Pro Thr His Gln Pro Pro Thr Pro Thr Pro
2290 2295 2300

His Gly Thr Thr Leu Ile Thr Gly Gly Thr Gly Ala Leu Ala Thr His
2305 2310 2315 2320

Leu Thr His His Leu Thr Thr His Gln Pro Thr Gln His Leu Leu Leu
2325 2330 2335

Thr Ser Arg Thr Gly Pro His Thr Pro His Ala Gln His Leu Thr Thr
2340 2345 2350

Gln Leu Gln Gln Lys Gly Ile His Leu Thr Ile Thr Thr Cys Asp Thr
2355 2360 2365

Ser Asn Pro Asp Gln Leu Gln Gln Leu Leu Asn Thr Ile Pro Pro Gln
2370 2375 2380

His Pro Leu Thr Thr Val Ile His Thr Ala Gly Ile Leu Asp Asp Ala
2385 2390 2395 2400

Thr Leu Thr Asn Leu Thr Pro Thr Gln Leu Asn Asn Val Leu Arg Ala
2405 2410 2415

Lys Ala His Ser Ala His Leu Leu His Gln Leu Thr Gln His Thr Pro
2420 2425 2430

Leu Asn Ala Phe Val Leu Tyr Ser Ser Ala Ala Ala Thr Phe Gly Ala
2435 2440 2445

Pro Gly Gln Ala Asn Tyr Ala Ala Ala Asn Ala Tyr Leu Asp Ala Leu
2450 2455 2460

Ala His His Arg His Thr His His Leu Pro Ala Thr Ser Ile Ala Trp
2465 2470 2475 2480

Gly Thr Trp Gln Gly Asn Gly Leu Ala Thr Gly Gln Val Ser Glu His
2485 2490 2495

Leu Arg Arg Arg Gly Met Phe Ala Met Pro Pro Glu Leu Ala Val Thr
2500 2505 2510

Ala Val Asp Gly Ala Ile Ala Ser Gly Arg Pro Ser Leu Leu Val Ala
2515 2520 2525

Asp Ile Asp Trp Lys Lys Leu Gly Pro Val Leu Ser Ser Lys Ser Ser
2530 2535 2540

Val Leu Leu Glu Asp Leu Pro Gln Ala Gln Gly Thr Glu Glu Ala Arg
2545 2550 2555 2560

Ser Thr Val Glu Gln Thr Glu Ser Thr Asn Leu Arg Gln Leu Leu Met
2565 2570 2575

Gly Arg Ser Arg Ser Glu Gln Glu Glu Glu Leu Leu Ser Leu Val Arg
2580 2585 2590

Ile His Ser Ala Ala Val Leu Gly Arg Asp Asp Ser Glu Ala Ile Pro
2595 2600 2605

Pro Gly Arg Leu Phe Arg Asp Leu Gly Phe Asp Ser Leu Ala Ala Val
2610 2615 2620

Glu Leu Arg Asn His Leu Ala Ala Gln Thr Glu Leu Ala Leu Pro Thr
2625 2630 2635 2640

Thr Leu Val Phe Asp Tyr Pro Ser Pro Thr Lys Leu Ala Gln Phe Leu
2645 2650 2655

Leu Ser Glu Ile Ala Glu Phe Gln Pro Asp Asn Ser Thr Pro Leu Pro
2660 2665 2670

Arg Pro Arg Ala Glu Leu Asp Glu Pro Ile Ala Ile Val Gly Met Ala
2675 2680 2685

Cys Arg Phe Pro Gly Gly Val Thr Ser Ala Asp Asp Phe Trp Asp Leu
2690 2695 2700

Ile Ser Ser Glu Gln Asp Ala Ile Gly Gly Phe Pro Thr Asp Arg Gly
2705 2710 2715 2720

Trp Asp Leu Asp Thr Leu Tyr Asp Pro Asp Pro Asp His Pro Gly Thr
2725 2730 2735

Cys Tyr Thr Arg Asn Gly Gly Phe Leu Tyr Asp Ala Gly His Phe Asp
2740 2745 2750

Ala Glu Phe Phe Gly Ile Ser Pro Arg Glu Ala Leu Ala Met Asp Pro
2755 2760 2765

Gln Gln Arg Leu Leu Leu Glu Thr Ala Trp Glu Thr Ile Glu His Ala
2770 2775 2780

Gly Ile Asn Pro His Thr Leu His Gly Thr Pro Thr Gly Val Phe Thr
2785 2790 2795 2800

Gly Thr Asn Gly Gln Asp His Ala Ala His Ile Arg Gln Ala Pro Ser
2805 2810 2815

Gly Thr Glu Gly Phe Val Leu Thr Gly Ala Ala Thr Ser Ile Ala Ser
2820 2825 2830

Gly Arg Ile Ser Tyr Ile Leu Gly Leu Glu Gly Pro Ala Val Thr Leu
2835 2840 2845

Asp Thr Ala Cys Ser Ser Ser Leu Val Ala Leu His Leu Ala Cys Gln
2850 2855 2860

Ser Leu Arg Ser Gly Glu Cys Thr Met Ala Leu Ala Gly Gly Ala Thr
2865 2870 2875 2880

Val Met Thr Thr Pro Ile Thr Phe Thr Glu Phe Ala Arg Gln Arg Gly
2885 2890 2895

Leu Ala Pro Asp Gly Arg Cys Lys Ala Phe Ser Ala Ala Ala Asp Gly
2900 2905 2910

Thr Gly Trp Gly Glu Gly Val Gly Met Leu Leu Val Glu Arg Leu Ser
2915 2920 2925

Asp Ala Arg Arg Asn Gly His Arg Val Leu Ala Val Val Arg Gly Ser
2930 2935 2940

Ala Val Asn Gln Asp Gly Ala Ser Asn Gly Leu Thr Ala Pro Asn Gly
2945 2950 2955 2960

Pro Ser Gln Gln Arg Val Ile Arg Gln Ala Leu Ala Asn Ala Asp Leu
2965 2970 2975

Thr Pro Ala Asp Val Asp Ala Val Glu Ala His Gly Thr Gly Thr Thr
2980 2985 2990

Leu Gly Asp Pro Ile Glu Ala Gln Ala Ile Leu Ala Thr Tyr Gly Gln
2995 3000 3005

Asp Arg Pro Gly Asn Gly Pro Leu Trp Leu Gly Ser Val Lys Ser Asn
3010 3015 3020

Val Gly His Thr Gln Ala Ala Ala Gly Val Ala Gly Val Ile Lys Met
3025 3030 3035 3040

Val Met Ala Leu Arg His Arg Thr Leu Pro Pro Thr Leu His Ala Asp
3045 3050 3055

Glu Pro Ser Pro His Val Asp Trp Ser Ala Gly Ala Val Gln Leu Leu
3060 3065 3070

Thr Glu Thr Val Pro Trp Pro Gly Gly Glu Gly Arg Pro Arg Arg Ala
3075 3080 3085

Gly Val Ser Ser Phe Gly Val Ser Gly Thr Asn Ala His Val Ile Leu
3090 3095 3100

Glu Glu Ala Pro Ala Asp Asp Val Pro Gly Gly Pro Pro Ala Asp Glu
3105 3110 3115 3120

Asp Ala Gly Ser Gly Glu Glu Ala Ala Ala Gly Ser Pro Gly Val Trp
3125 3130 3135

Pro Trp Leu Val Ser Ala Lys Ser Gln Pro Ala Leu Arg Ala Gln Ala
3140 3145 3150

Gln Ala Leu His Ala His Leu Thr Asp His Pro Gly Leu Asp Leu Ala
3155 3160 3165

Asp Val Gly Tyr Thr Leu Ala His Ala Arg Ala Val Phe Asp His Arg
3170 3175 3180

Ala Thr Leu Ile Ala Ala Asp Arg Asp Thr Phe Leu Gln Ala Leu Gln
3185 3190 3195 3200

Ala Leu Ala Ala Gly Glu Pro His Pro Ala Val Ile His Ser Ser Ala
3205 3210 3215

Pro Gly Gly Thr Gly Thr Gly Glu Ala Ala Gly Lys Thr Ala Phe Ile
3220 3225 3230

Cys Ser Gly Gln Gly Thr Gln Arg Pro Gly Met Ala His Gly Leu Tyr
3235 3240 3245

His Thr His Pro Val Phe Ala Ala Ala Leu Asn Asp Ile Cys Thr His
3250 3255 3260

Leu Asp Pro His Leu Asp His Pro Leu Leu Pro Leu Leu Thr Gln Asn
3265 3270 3275 3280

Asp Asn Asp Asn Asp Asn Glu Asp Ala Ala Ala Leu Leu Gln Gln Thr
3285 3290 3295

Pro Tyr Ala Gln Pro Ala Leu Phe Ala Phe Gln Val Ala Leu His Arg
3300 3305 3310

Leu Leu Thr Asp Gly Tyr His Ile Thr Pro His Tyr Tyr Ala Gly His
3315 3320 3325

Ser Leu Gly Glu Ile Thr Ala Ala His Leu Ala Gly Ile Leu Thr Leu
3330 3335 3340

Thr Asp Ala Thr Thr Leu Ile Thr Gln Arg Ala Thr Leu Met Gln Thr
3345 3350 3355 3360

Met Pro Pro Gly Thr Met Thr Thr Leu His Thr Thr Pro His His Ile
3365 3370 3375

Thr His His Leu Thr Ala His Glu Asn Asp Leu Ala Ile Ala Ala Ile
3380 3385 3390

Asn Thr Pro Thr Ser Leu Val Ile Ser Gly Thr Pro His Thr Val Gln
3395 3400 3405

His Ile Thr Thr Leu Cys Gln Gln Gln Gly Ile Lys Thr Lys Thr Leu
3410 3415 3420

Pro Thr Asn His Ala Phe His Ser Pro His Thr Asn Pro Ile Leu Asn
3425 3430 3435 3440

Gln Leu His Gln His Thr Gln Thr Leu Thr Tyr His Pro Pro His Thr
3445 3450 3455

Pro Leu Ile Thr Ala Asn Thr Pro Pro Asp Gln Leu Leu Thr Pro His
3460 3465 3470

Tyr Trp Thr Gln Gln Ala Arg Asn Thr Val Asp Tyr Ala Thr Thr Thr
3475 3480 3485

Gln Thr Leu His Gln His Gly Val Thr Thr Tyr Ile Glu Leu Gly Pro
3490 3495 3500

Asp Asn Thr Leu Thr Thr Leu Thr His His Asn Leu Pro Asn Thr Pro
3505 3510 3515 3520

Thr Thr Thr Leu Thr Leu Thr His Pro His His His Pro Gln Thr His
3525 3530 3535

Leu Leu Thr Asn Leu Ala Lys Thr Thr Thr Thr Trp His Pro His His
3540 3545 3550

Tyr Thr His His His Asn Gln Pro His Thr His Thr His Leu Asp Leu
3555 3560 3565

Pro Thr Tyr Pro Phe Gln His His His Tyr Trp Leu Glu Leu Pro Ser
3570 3575 3580

Ala Gln Thr Ser Pro Gly Gln Arg Arg Ser Arg Arg Ser Ala Pro Asp
3585 3590 3595 3600

Thr Ala Glu Ser Glu Phe Trp Asp Ala Val Asn Glu Glu Asp Leu Gln
3605 3610 3615

Replacement Sheet

Ser Leu Ala Glu Thr Leu Asp Ile Asp Ala Ser Ala Leu Asp Thr Val
3620 3625 3630

Val Pro Ala Leu Ser Ala Trp His Arg His Gln His Asp Gln Ala Arg
3635 3640 3645

Ile Asn Thr Trp Thr Tyr Gln Glu Thr Trp Lys Pro Leu Thr Leu Pro
3650 3655 3660

Thr Thr His Gln Pro His Gln Thr Trp Leu Ile Ala Ile Pro Glu Thr
3665 3670 3675 3680

Gln Thr His His Pro His Ile Thr Asn Ile Leu Thr Asn Leu His His
3685 3690 3695

His Gly Ile Thr Pro Ile Pro Leu Thr Val Asn His Thr His Thr Asn
3700 3705 3710

Pro Gln His Leu His His Thr Leu His His Thr Arg Gln Gln Ala Gln
3715 3720 3725

Asn His Thr Thr Gly Pro Ile Thr Gly Leu Leu Ser Leu Leu Ala Leu
3730 3735 3740

Asp Glu Thr Pro His Pro His His Pro His Thr Pro Thr Gly Thr Leu
3745 3750 3755 3760

Leu Asn Leu Thr Leu Pro Gln Thr His Thr Gln Thr His Pro Pro Thr
3765 3770 3775

Pro Leu Trp Tyr Ala Thr Thr Asn Ala Thr Thr Thr His Pro Asn Asp
3780 3785 3790

Pro Leu Thr His Pro Thr Gln Ala Gln Thr Trp Gly Leu Ala Arg Thr
3795 3800 3805

Thr Leu Leu Glu His Pro Thr His Thr Ala Gly Ile Ile Asp Leu Pro
3810 3815 3820

Thr Thr Pro Thr Pro His Thr Leu His His Leu Thr Gln Thr Leu Thr
3825 3830 3835 3840

Gln Pro His His Gln Thr Gln Leu Ala Ile Arg Thr Thr Gly Thr His
3845 3850 3855

Thr Arg Arg Leu Thr Pro Thr Thr Leu Thr Pro Thr His Gln Pro Pro
3860 3865 3870

Thr Pro Thr Pro His Gly Thr Thr Leu Ile Thr Gly Gly Thr Gly Ala
3875 3880 3885

Leu Ala Thr His Leu Thr His His Leu Thr Thr His Gln Pro Thr Gln
3890 3895 3900

His Leu Leu Leu Thr Ser Arg Thr Gly Pro His Thr Pro His Ala Gln
3905 3910 3915 3920

His Leu Thr Thr Gln Leu Gln Gln Lys Gly Ile His Leu Thr Ile Thr
3925 3930 3935

Thr Cys Asp Thr Ser Asn Pro Asp Gln Leu Gln Gln Leu Leu Asn Thr
3940 3945 3950

Ile Pro Pro Gln His Pro Leu Thr Thr Val Ile His Thr Ala Gly Val
3955 3960 3965

Asn Leu Phe Ala Pro Val Ser Glu Thr Asp Ala Glu Ser Phe Ser Ser
3970 3975 3980

Val Thr Ala Ala Lys Ala Thr Gly Ala Ala Ile Leu His Glu Leu Leu
3985 3990 3995 4000

Leu Asp His Glu Thr Leu Glu His Phe Ile Leu Phe Ser Ser Gly Ala
4005 4010 4015

Gly Ala Trp Gly Ser Gly Asn Gln Cys Ala Tyr Ser Ala Ala Asn Ala
4020 4025 4030

Tyr Leu Asp Ala Leu Ala Thr His Arg Gln Thr His Gly Leu Pro Gly
4035 4040 4045

Ala Ser Ile Ala Trp Gly Pro Trp Ala Gly Lys Gly Met Ser Ala Gly
4050 4055 4060

Asp Ala Ala His Gly Tyr Leu Glu Lys Arg Gly Ile Leu Pro Met Glu
4065 4070 4075 4080

Pro Arg Met Ala Leu Ala Ala Phe His Arg Ala Arg Ala Gln Arg Pro
4085 4090 4095

Asn Ser Asn Leu Ile Ile Ala Asp Ile Asp Trp Glu Arg Phe Val Pro
4100 4105 4110

Ala Phe Thr Ala Arg Arg His Ser Pro Leu Ile Glu Asp Ile Pro Glu
4115 4120 4125

Val Arg Gln Ala Ala Gln Glu Leu Glu Ala Ala Ala Ser Thr Ala Lys
4130 4135 4140

Thr Thr Thr Ala Gln Pro Ile Ala Thr Ser Leu Arg Glu Arg Leu Ala
4145 4150 4155 4160

Arg Leu Thr Ser Ser Lys Gln Asn Gln Val Leu Leu Gly Leu Ile Arg
4165 4170 4175

Thr Gly Ile Cys Thr Val Leu Gly Leu Arg Asn Pro Glu Gly Ile Glu
4180 4185 4190

Asp Gln Arg Ala Phe Arg Asp Leu Gly Phe Asp Ser Leu Thr Ser Ala
4195 4200 4205

Gln Phe Ser Lys Glu Leu Ala Lys Glu Thr Gly Leu Pro Leu Pro Pro
4210 4215 4220

Ser Leu Val Phe Asp Tyr Pro Thr Pro Gln Glu Cys Ala Ala His Leu
4225 4230 4235 4240

Arg Thr Gln Leu Val Asp Leu Asp Asp Glu Glu Asp Ala Ala Leu Ser
4245 4250 4255

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Asn Ala Leu Pro Gln Val Ala His Arg Arg Thr Val Glu Asp Glu Pro
4260 4265 4270

Ile Ala Ile Ile Gly Met Ala Cys Arg Phe Pro Gly Gly Val Arg Ser
4275 4280 4285

Ala Asp Asp Leu Trp Glu Leu Leu Ala Ser Gly Lys Asp Ala Ile Gly
4290 4295 4300

Val Phe Pro Thr Asp Arg Gly Trp Asp Leu Asp Thr Leu Tyr Asp Pro
4305 4310 4315 4320

Asp Pro Asp His Pro Gly Thr Cys Tyr Thr Arg Asn Gly Gly Phe Leu
4325 4330 4335

Tyr Gly Ala Gly His Phe Asp Ala Glu Phe Phe Gly Ile Ser Pro Arg
4340 4345 4350

Glu Ala Leu Ala Met Asp Pro Gln Gln Arg Leu Leu Leu Glu Thr Ala
4355 4360 4365

Trp Glu Thr Ile Glu His Ala Gly Ile Asn Pro His Thr Leu His Gly
4370 4375 4380

Thr Pro Thr Gly Val Phe Ala Gly Ile Asn Ala Gln Asp His Ala Ala
4385 4390 4395 4400

His Ile Arg Gln Ser Arg Asp Val Glu Thr Ile Glu Gly Tyr Ala Leu
4405 4410 4415

Thr Gly Ser Ser Gly Ser Val Ala Ser Gly Arg Val Ala Tyr Thr Leu
4420 4425 4430

Gly Leu Glu Gly Pro Ala Val Ser Val Asp Thr Ala Cys Ser Ser Ser
4435 4440 4445

Leu Val Ala Leu His Trp Ala Ala Gln Ala Leu Arg Ala Gly Glu Cys
4450 4455 4460

Ser Met Ala Leu Ala Gly Gly Val Thr Val Met Ser Ser Pro Gly Thr
4465 4470 4475 4480

Phe Val Glu Phe Ser Arg Gln Arg Gly Leu Ala Ala Asp Gly Arg Cys
4485 4490 4495

Lys Ala Tyr Ser Ala Ala Ala Asp Gly Thr Gly Trp Ala Glu Gly Val
4500 4505 4510

Gly Met Leu Leu Val Glu Arg Leu Ser Asp Ala Arg Arg Asn Gly His
4515 4520 4525

Arg Val Leu Ala Val Val Arg Gly Ser Ala Val Asn Gln Asp Gly Ala
4530 4535 4540

Ser Asn Gly Leu Thr Ala Pro Asn Gly Pro Ser Gln Gln Arg Val Ile
4545 4550 4555 4560

Arg Gln Ala Leu Ala Asn Ala Gly Leu Thr Pro Ala Asp Val Asp Ala
4565 4570 4575

Val Glu Gly His Gly Thr Gly Thr Thr Leu Gly Asp Pro Ile Glu Ala
4580 4585 4590

Gln Ala Leu Leu Ala Ala Tyr Gly Gln His Arg Pro His His Arg Pro
4595 4600 4605

Leu Trp Leu Gly Ser Leu Lys Ser Asn Ile Gly His Ala Gln Ala Ala
4610 4615 4620

Ala Gly Val Gly Gly Val Ile Lys Met Val Met Ala Leu Arg Asn Gly
4625 4630 4635 4640

Leu Leu Pro Gln Thr Leu His Val Asp Glu Pro Thr Pro Gln Val Asp
4645 4650 4655

Trp Ser Thr Gly Ala Val Gln Leu Leu Thr Gln Pro Val Pro Trp Pro
4660 4665 4670

Ala Asp Pro Ala Gly Arg Pro Arg His Ala Gly Val Ser Ser Phe Gly
4675 4680 4685

Val Ser Gly Thr Asn Ala His Ile Ile Leu Glu Glu Ala Pro Thr Pro
4690 4695 4700

Gln Asp Ser Asp Thr Asp Asp Glu Pro Pro Ala Asn Ala Pro Ala Leu
4705 4710 4715 4720

Pro His Pro Leu Pro Leu Pro Val Pro Val Ser Ala Arg Ser Glu Ala
4725 4730 4735

Gly Leu Arg Ala Gln Ala Gln Ala Leu Arg Gln Tyr Val Ala Ala Arg
4740 4745 4750

Pro Asp Met Ser Pro Ala Asp Ile Gly Ala Gly Leu Ala Arg Gly Arg
4755 4760 4765

Ala Val Leu Glu His Arg Ala Val Ile Leu Ala Ala Asp Arg Glu Glu
4770 4775 4780

Leu Ala Gln Ala Leu Thr Ala Leu Ala Ala Gly Glu Pro His Pro His
4785 4790 4795 4800

Ile Thr Thr Gly His Thr Arg Gly Gly Asp Arg Gly Gly Val Val Phe
4805 4810 4815

Val Phe Pro Gly Gln Gly Gly Gln Trp Ala Gly Met Gly Leu Thr Leu
4820 4825 4830

Leu Thr Ser Ser Pro Val Phe Ala Glu His Ile Asp Ala Cys Glu Lys
4835 4840 4845

Ala Leu Thr Pro Trp Val Pro Trp Ser Leu Thr Asp Ile Leu His Arg
4850 4855 4860

Asp Pro Asp Asp Pro Ala Trp Gln Gln Ala Asp Val Val Gln Pro Val
4865 4870 4875 4880

Leu Phe Ser Ile Met Val Ser Leu Ala Ala Leu Trp Arg Ser Tyr Gly
4885 4890 4895

Ile Glu Pro Asp Ala Val Leu Gly His Ser Gln Gly Glu Ile Ala Ala
4900 4905 4910

Ala His Ile Cys Gly Ala Leu Ser Leu Lys Asp Ala Ala Lys Thr Val
4915 4920 4925

Ala Leu Arg Ser Arg Ala Leu Ala Ala Val Arg Gly Arg Gly Ala Met
4930 4935 4940

Ala Ser Leu Pro Leu Pro Ala Gln Asp Val Gln Gln Leu Ile Ser Glu
4945 4950 4955 4960

Arg Trp Glu Gly Gln Leu Trp Val Ala Ala Leu Asn Gly Pro His Ser
4965 4970 4975

Thr Thr Val Ser Gly Asp Thr Lys Ala Val Asp Glu Val Leu Ala His
4980 4985 4990

Cys Thr Asp Thr Gly Leu Arg Ala Lys Arg Ile Pro Val Asp Tyr Ala
4995 5000 5005

Ser His Cys Pro His Val Gln Pro Leu His Asp Glu Leu Leu His Leu
5010 5015 5020

Leu Gly Asp Ile Thr Pro Gln Pro Ser Thr Val Pro Phe Phe Ser Thr
5025 5030 5035 5040

Val Glu Gly Thr Trp Leu Asp Thr Thr Thr Leu Asp Ala Ala Tyr Trp
5045 5050 5055

Tyr Arg Asn Leu His Gln Pro Val Arg Phe Ser His Ala Ile Gln Thr
5060 5065 5070

Leu Thr Asp Asp Gly His Arg Ala Phe Ile Glu Ile Ser Pro His Pro
5075 5080 5085

Thr Leu Val Pro Ala Ile Glu Asp Thr Thr Glu Asn Thr Thr Glu Asn
5090 5095 5100

Ile Thr Ala Thr Gly Ser Leu Arg Arg Gly Asp Asn Asp Thr His Arg
5105 5110 5115 5120

Phe Leu Thr Ala Leu Ala His Thr His Thr Thr Gly Ile Gly Thr Pro
5125 5130 5135

Thr Thr Trp His His His Tyr Thr Gln Thr His Pro His Pro Asn Pro
5140 5145 5150

His Thr His Leu Asp Leu Pro Thr Tyr Pro Phe Gln His Gln His Tyr
5155 5160 5165

Trp Leu Gln Pro Pro Thr Thr Thr Thr Asp Leu Thr Thr Thr Gly Leu
5170 5175 5180

Thr Pro Thr His His Pro Leu Leu Thr Ala Thr Leu Thr Leu Ala Asp
5185 5190 5195 5200

Asn Asn Thr Gln Leu Leu Thr Gly Arg Leu Ser Leu Arg Thr His Pro
5205 5210 5215

Trp Leu Thr Asp His Thr Val Ala Gly Met Val Leu Leu Pro Gly Thr
5220 5225 5230

Ala Leu Leu Glu Leu Ala Leu Gln Ala Gly Glu Arg Val Asp Cys Pro
5235 5240 5245

Arg Val Glu Glu Leu Thr Leu His Ala Pro Leu Val Ile Pro His Thr
5250 5255 5260

Glu Asp Val Thr Leu Gln Val Thr Val Arg Ala Ala Asp Glu Ser Gly
5265 5270 5275 5280

His Arg Ala Leu Ala Ile His Ser Tyr Ser Gly Thr Ala Ser Ser Ala
5285 5290 5295

Asp Arg Glu Trp Thr Arg His Ala Thr Gly Leu Leu Thr His His Ala
5300 5305 5310

Asp Thr Asp His Arg Ala Asp Thr His Thr Asp Ala Cys Leu Gly Gly
5315 5320 5325

Ser Trp Pro Pro Pro Gly Ala Gln Pro Ile Glu Leu Gly Asp Val Tyr
5330 5335 5340

Gly Arg Met Ala Ala Asp Ser Asp Ile Ala Tyr Gly Pro Val Phe Gln
5345 5350 5355 5360

Gly Leu His Ala Ala Trp Arg Phe Gly Asp Asp Val Leu Ala Glu Val
5365 5370 5375

Arg Leu Pro Glu Glu Ala Leu Arg Asp Ala Pro Ala Ala Ala Phe Gly
5380 5385 5390

Val His Pro Ala Leu Leu Asp Ala Ala Leu His Ala Thr Ala Leu Thr
5395 5400 5405

Pro Gln Asn Gly Asp Gly Ser Thr Glu Asn Val Ala Gln Glu Ser Met
5410 5415 5420

Pro Asp Arg Ala Ala His Gln Ala Arg Leu Pro Phe Ser Trp Ser Gly
5425 5430 5435 5440

Val Ser Leu His Thr Ala Gly Ser Ser Val Leu Arg Val Arg Leu Ser
5445 5450 5455

Arg Ser Pro Gln His Gly Asn Ala Val Ala Leu Thr Ala Ala Asp Glu
5460 5465 5470

Asp Gly Arg Pro Val Val Thr Ile Glu Ser Leu Ala Leu Arg Pro Val
5475 5480 5485

Ser Thr Glu Glu Leu Arg Ala Ala Ala Asp Arg Thr Pro Glu His Glu
5490 5495 5500

Ser Leu Phe Arg Leu Asp Trp Val Ser Val Pro Val Pro Ala Asn Ala
5505 5510 5515 5520

Pro Ser Pro Thr Ala Asp Arg Pro Trp Ala Val Ile Gly Ala Gly Leu
5525 5530 5535

Pro His Leu Pro Gly Leu Thr Glu His Glu His Val Thr Ala Tyr Asp
5540 5545 5550

Glu Pro Ala Asp Leu Leu Leu Ala Leu Asp Arg Gly Ala Pro Pro Pro
5555 5560 5565

Gly Val Leu Val Val Gly Gly Val Ala His Thr Glu Ala Arg Glu Tyr
5570 5575 5580

Ser Ala Glu Ala Pro Gly Glu Arg Gly Thr Glu Ala Cys Glu Ala Arg
5585 5590 5595 5600

Pro Asp Val Val His Val Gly Val Val His Thr Ala Ala Val His Ala
5605 5610 5615

Ala Ala Ala Gln Met Leu Ala Arg Leu Gln Ala Trp Leu Gly Asp Glu
5620 5625 5630

Arg Leu Ala Asp Ser Arg Leu Leu Val Leu Thr Cys Gly Ala Val Ala
5635 5640 5645

Arg Ala Ser Gly Asp Asp Ala Thr Asp Leu Pro Gly Ala Ala Val Trp
5650 5655 5660

Gly Leu Val Arg Ser Ala Gln Ser Glu His Pro Asp Arg Ile Thr Leu
5665 5670 5675 5680

Leu Asp Phe Glu Arg Gly Thr Glu Ala Glu Pro Gly Gln Leu Ala Thr
5685 5690 5695

Ala Leu Asn Cys Gly Glu Arg Gln Leu Ala Val Arg Pro Gly Gly Leu
5700 5705 5710

Phe Thr Pro Arg Leu Val Arg Ala Pro Arg Val Ala Asp Ala Val Pro
5715 5720 5725

Ala Val Pro Ala Val Ala Val Pro Ser Ala Gly His Ala Ala Val Pro
5730 5735 5740

Ala Ala Gly Pro Phe Leu Pro Gly Gly Thr Val Leu Ile Thr Gly Gly
5745 5750 5755 5760

Thr Gly Val Leu Gly Arg Leu Val Ala Arg His Leu Val Glu Ala His
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Gly Val Arg His Leu Leu Leu Ala Gly Arg Arg Gly Pro Asp Ala Glu
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Gly Ala Pro Glu Leu Arg Ala Glu Leu Gly Gly Leu Gly Ala Thr Val
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Glu Val Val Ala Cys Asp Ala Ala Asp Arg Gln Gln Leu Ala Asp Leu
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Leu Thr Arg Ile Pro Asp Asp Arg Pro Leu Thr Gly Val Val His Ser
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Ala Gly Ile Leu Asp Asp Gly Val Ile Thr Ser Leu Ser Pro Glu Arg
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Leu Gly Ala Val Leu Arg Ala Lys Ala Asp Ala Ala Leu Leu Leu Asp
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Glu Leu Thr Arg Gly Ala Glu Leu Ser Ala Phe Val Met Phe Ser Ser
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Ala Ser Ala Val Val Gly Ser Pro Gly Gln Gly Asn Tyr Ala Ala Ala
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Asn Ala Val Leu Asp Phe Leu Ala His Arg Arg Arg Ala Glu Gly Leu
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Pro Ala Val Ser Leu Ala Trp Gly Leu Trp Glu Glu Gly Thr Gly Met
5925 5930 5935

Thr Gly His Leu Asp Val Asp Asp His Ala Arg Ile Ser Arg Ala Gly
5940 5945 5950

Met Arg Pro Leu Pro Thr Ala Glu Ala Leu Ala Leu Phe Asp Ala Ala
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Leu Ala Asp Gly Glu Pro Phe Leu Met Pro Ala Arg Leu Asp Leu Thr
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Ala Val Arg Ser Gly Ala Ala Ser Ala Pro Val Pro Pro Leu Leu Gln
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Gly Leu Leu Gln Leu Pro Arg Ser Arg Ser Ala Ala Ala Ala Pro Gly
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His Gly Ala Pro Ala Ala Asp Glu Ala Ala Ala Trp Arg Glu Arg Leu
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Ala Arg Gln Ser Ala Gly Glu Arg Arg Gln Ala Leu Leu Arg Leu Val
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Arg Ser His Val Ala Ala Val Leu Gly His Ser Gly Ala Asp Gly Ile
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Asp Ala Ser Arg Ala Phe Arg Glu Leu Gly Phe Asp Ser Leu Thr Ala
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Val Glu Leu Arg Asn Arg Leu Thr Ala Ala Thr Gly Leu Arg Leu Arg
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Ala Thr Leu Ala Phe Asp Phe Pro Thr Pro Ala Ala Leu Ala Glu His
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Leu Gly Glu Arg Leu Leu Pro Asp Gln Glu Ala Thr Gly Glu Gln Ala
6115 6120 6125

Gly Asp Gln Leu Ser Gly Gly Ser Glu Glu Asp Val Arg Ser Leu Leu
6130 6135 6140

Thr Ser Ile Pro Ile Gly Arg Leu Arg Asp Ala Gly Leu Leu Gly Pro
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Leu Leu Thr Leu Ala Asp Thr Gly Arg Gly Ala Ser Gly Ala Ala Ala
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Gly Pro Glu Asp Ala Pro Pro Ser Gly Gln Asp Thr Pro Ala Pro Val
          6180                6185                6190

Ser Ile Asp Glu Met Asp Ile Asp Asp Leu Met Asp Leu Ala His Gly
       6195                6200                6205

His Gly Thr Ala Pro Ala Arg Glu Pro Ala Asp Ala Glu Asp Ser Ser
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Ser Ser Arg Asn Arg Thr His His Thr His Glu Gly Glu Thr Ala
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<212> PRT
<213> Streptomyces avermitilis

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             20                  25                  30

Gln Glu Pro Ile Ala Ile Val Gly Met Ala Cys Arg Phe Pro Gly Gly
         35                  40                  45

Val Glu Ser Ala Glu Asp Phe Trp Glu Leu Ile Ala Ser Gly Arg Asp
     50                  55                  60

Ala Val Gly Glu Phe Pro Val Asp Arg Gly Trp Asp Val Glu Ala Phe
 65                  70                  75                  80

Tyr Asp Pro Glu Pro Gly Arg Ala Gly Ser Ser Tyr Thr Arg Arg Gly
                 85                  90                  95

Gly Phe Leu Glu Gly Ala Ala Glu Phe Asp Ala Gly Phe Phe Gly Ile
            100                 105                 110

Ser Pro Arg Glu Ala Leu Ala Met Asp Pro Gln Gln Arg Leu Met Leu
        115                 120                 125

Glu Val Ser Trp Glu Ala Leu Glu Arg Ala Gly Ile Asp Pro Ala Thr
    130                 135                 140

Leu Arg Gly Ser Arg Thr Gly Val Phe Ala Gly Leu Met Ser Gln Asp
145                 150                 155                 160

Tyr Ala Thr Arg Leu Leu Ser Val Pro Asp Asp Leu Ala Gly Tyr Leu
                165                 170                 175

Gly Asn Gly Asn Ala Gly Ser Ile Leu Ser Gly Arg Val Ala Tyr Thr
            180                 185                 190

Phe Gly Phe Glu Gly Pro Ala Val Thr Val Asp Thr Ala Cys Ser Ser
        195                 200                 205

Ser Leu Val Ala Leu His Leu Ala Cys Gln Ser Leu Arg Thr Gly Glu
    210                 215                 220
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Ser Ser Phe Ala Leu Ala Gly Gly Val Thr Val Met Ser Thr Pro Gly
225 230 235 240

Met Phe Val Glu Phe Ser Arg Gln Arg Gly Leu Ser Pro Asp Gly Arg
245 250 255

Cys Lys Ala Tyr Ala Ser Ala Ala Asp Gly Thr Gly Met Ser Glu Gly
260 265 270

Val Gly Ile Leu Leu Leu Glu Arg Leu Ser Glu Ala Glu Arg Arg Gly
275 280 285

His Arg Val Leu Ala Val Val Arg Gly Ser Ala Val Asn Gln Asp Gly
290 295 300

Ala Ser Asn Gly Leu Thr Ala Pro Asn Gly Pro Ser Gln Gln Arg Val
305 310 315 320

Ile Arg Gln Ala Leu Ala Cys Ala Gly Leu Ser Val Ala Asp Val Asp
325 330 335

Val Val Glu Gly His Gly Thr Gly Thr Thr Leu Gly Asp Pro Ile Glu
340 345 350

Ala Gln Ala Leu Leu Ala Thr Tyr Gly Gln Arg Ala Gly Asp Thr Pro
355 360 365

Val Trp Leu Gly Ser Val Lys Ser Asn Ile Gly His Ala Gln Ala Ala
370 375 380

Ala Gly Val Ala Gly Val Ile Lys Met Val Met Ala Leu Arg Ala Gly
385 390 395 400

Val Leu Pro Arg Thr Leu His Val Asp Glu Pro Ser Ser Gln Val Asp
405 410 415

Trp Ser Ser Gly Ser Val Arg Val Leu Ala Asp Glu Val Glu Trp Pro
420 425 430

Gly Val Glu Gly Arg Leu Arg Arg Ala Gly Val Ser Ala Phe Gly Val
435 440 445

Ser Gly Thr Asn Ala His Val Ile Leu Glu Glu Ala Ser Gly Gly Ala
450 455 460

Gly Gly Gly Ala Gly Arg Leu Gln Glu Leu Gly Pro Gly Val Val Ser
465 470 475 480

Gly Ser Gly Val Val Pro Trp Val Val Ser Ala Arg Ser Glu Leu Ala
485 490 495

Leu Arg Gly Gln Ala Arg Arg Leu Arg Gly Val Val Ala Val Gly Gly
500 505 510

Gly Ala Asp Gly Val Gly Val Ser Pro Ala Gly Val Gly Arg Ala Leu
515 520 525

Val Ser Glu Arg Ser Val Phe Glu His Arg Ala Val Val Val Ala Glu
530 535 540

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Asp Arg Asp Glu Phe Leu His Ala Leu Asp Ala Leu Ala Gly Gly Arg
545                 550                 555                 560

Pro Val Pro Gly Val Val Glu Gly Arg Thr Thr Ser Gly Glu Leu Ala
                565                 570                 575

Val Leu Phe Ala Gly Gln Gly Thr Gln Arg Ala Gly Met Gly Arg Glu
            580                 585                 590

Leu Tyr Glu Ala Tyr Pro Val Phe Ala Gln Ala Ile Asp Glu Ile Cys
        595                 600                 605

Ala Glu Ala Asp Thr Ala Arg Thr Asp Pro Gly Ala Pro Gly Leu Arg
    610                 615                 620

Asp Val Leu Phe Ala Pro Gln Asp Ser Pro Glu Gly Arg Leu Ile Glu
625                 630                 635                 640

Asp Thr Gly Phe Ala Gln Pro Ala Leu Phe Ala Phe Glu Val Ala Leu
                645                 650                 655

Phe Arg Leu Leu Glu Thr Trp Gly Leu Thr Pro Asp Tyr Val Leu Gly
            660                 665                 670

His Ser Val Gly Glu Leu Ala Ala Ala His Val Ala Gly Met Leu Cys
        675                 680                 685

Leu Ala Asp Ala Val Ala Leu Val Val Ala Arg Gly Arg Leu Met Gln
    690                 695                 700

Gly Leu Pro Ser Gly Gly Ala Met Val Ala Ile Glu Ala Ser Glu Asp
705                 710                 715                 720

Glu Ile Leu Pro Leu Pro Asp Glu Tyr Ala Ser Arg Val Ala His Ala
                725                 730                 735

Ala Val Asn Gly Pro Arg Ser Ile Val Leu Ser Gly Asp Glu Asp Ala
            740                 745                 750

Val Leu Asp Leu Ala Gln Gln Trp Ala Ala Arg Gly Arg Arg Thr Arg
        755                 760                 765

Arg Leu Arg Thr Ser His Ala Phe His Ser Pro His Met Asp Ala Met
    770                 775                 780

Leu Gly Asp Phe Arg Arg Ala Ala Glu Gln Val Thr Phe Ser Ala Pro
785                 790                 795                 800

Arg Ile Pro Val Val Ser Asn Val Thr Gly Ala Pro Leu Pro Ala Glu
                805                 810                 815

Thr Met Cys Thr Pro Asp Tyr Trp Val Glu His Ala Arg Ser Thr Val
            820                 825                 830

Arg Phe Ala Asp Gly Ile Ser Trp Leu Gln Glu Gln Gly Val Thr Thr
        835                 840                 845

Cys Leu Glu Ile Gly Pro Asp Gly Thr Leu Ser Ala Leu Ala Gln Asp
    850                 855                 860
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Ser Leu Ser Ala Pro Ala Arg Ala Ile Pro Ala Leu Arg Pro Asp Gln
865 870 875 880

Pro Glu Ala Arg Ser Val Met Thr Ala Leu Ala Glu Leu Phe Val Ala
885 890 895

Gly Thr Ala Val Glu Trp Ala Gly Val Phe Glu Gly Thr Ala Arg Glu
900 905 910

Val Gly Asp Gly Cys Gly Val Glu Leu Pro Thr Tyr Ala Phe Glu Arg
915 920 925

Glu Arg Phe Trp Leu Asp Val Glu Glu Gly Ser Ala Gly Gly Ser Gly
930 935 940

Val Ser Gly Met Trp Gly Gly Pro Leu Trp Glu Ala Val Glu Cys Gly
945 950 955 960

Asp Ala Gly Val Val Ala Ser Leu Leu Gly Val Asp Glu Gly Ala Ser
965 970 975

Leu Gly Ala Val Val Ser Ala Leu Gly Glu Trp Gly Arg Val Arg His
980 985 990

Glu Arg Glu Val Val Asp Gly Trp Arg Tyr Arg Glu Val Trp Arg Pro
995 1000 1005

Val Ser Gly Gly Gly Val Gly Gly Leu Ser Gly Ala Trp Leu Val Val
1010 1015 1020

Ser Glu Gly Glu Ala Gly Pro Val Asp Val Val Ala Glu Gly Leu Glu
1025 1030 1035 1040

Arg Cys Gly Ala Arg Val Val Arg Val Glu Val Glu Ala Gly Cys Val
1045 1050 1055

Ser Arg Glu Val Leu Ala Gly His Leu Arg Glu Ala Val Asp Gly Glu
1060 1065 1070

Ala Val Gly Gly Val Val Ser Leu Val Gly Trp Gly Ser Gly Val Val
1075 1080 1085

Gln Ala Gly Val Ala Ser Val Gly Leu Val Gln Ala Leu Gly Asp Val
1090 1095 1100

Gly Val Gly Ala Arg Leu Trp Cys Val Thr Gly Gly Ala Val Ser Val
1105 1110 1115 1120

Gly Gly Arg Asp Ala Val Trp Gly Pro Ala Ser Gly Val Val Trp Gly
1125 1130 1135

Leu Gly Arg Val Val Gly Ala Glu Ala Pro Asp Arg Trp Gly Gly Leu
1140 1145 1150

Val Asp Val Pro Glu Leu Val Asp Glu Arg Val Val Asp Gly Leu Val
1155 1160 1165

Gly Val Leu Ala Gly Val Gly Gly Gly Gly Glu Ser Glu Phe Ala Val
1170 1175 1180

Arg Ser Ser Gly Ala Phe Val Arg Arg Leu Val Arg Ala Pro Leu Glu
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Glu Ala Val Ala Glu Arg Glu Trp Arg Pro Arg Gly Thr Val Leu Val
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Thr Gly Gly Thr Gly Glu Leu Gly Ala His Val Ala Arg Trp Met Ala
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Arg Arg Gly Ala Glu His Leu Leu Leu Val Ser Arg Arg Gly Glu Ser
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Ala Gln Gly Val Glu Glu Leu Arg Ala Asp Leu Met Gly Leu Gly Ala
1250 1255 1260

Arg Val Ser Val Val Ala Cys Asp Ala Ala Asp Arg Glu Ala Leu Ala
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Glu Val Leu Arg Ser Ala Val Pro Ala Glu Cys Pro Leu Gly Val Val
1285 1290 1295

Val His Ala Ala Gly Val Val Asp Asp Gly Val Leu Glu Gly Leu Ser
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Ser Glu Arg Val Thr Gly Val Leu Arg Ala Lys Ala Leu Ala Ala Trp
1315 1320 1325

Asn Leu His Glu Leu Thr Arg Gly Ala Asp Leu Ser Gly Phe Val Val
1330 1335 1340

Phe Ser Ser Ala Ala Ala Thr Phe Gly Pro Ala Gly Gln Gly Ser Tyr
1345 1350 1355 1360

Ala Ala Ala Asn Ala Tyr Val Glu Ala Ile Val Arg His Arg Arg Gly
1365 1370 1375

Glu Gly Leu Pro Gly Leu Ala Val Ala Trp Gly Pro Trp Ala Gly Gly
1380 1385 1390

Gly Met Ala Glu Gly Ala Val Gly Gln Met Arg Arg Arg Gly Leu Ala
1395 1400 1405

Ala Met Thr Pro Glu Thr Ala Leu Val Ala Leu Gly Gln Ala Leu Asp
1410 1415 1420

His Asp Glu Thr Cys Val Thr Val Ala Asp Ile Asp Trp Asp Arg Phe
1425 1430 1435 1440

Thr Ala Asn Ser Leu Pro Gly Ser Arg Leu Ser Pro Leu Ile Ser Asp
1445 1450 1455

Ile Pro Glu Ala Arg Leu Ala Arg Glu Thr Thr Gly Leu Asp Thr Ala
1460 1465 1470

Thr Ala Ser Pro Asp Ser Phe Ser Ala Arg Leu Lys Ala Met Asp Thr
1475 1480 1485

Ala Glu Gln Glu Arg Ala Leu Leu Asp Leu Val Arg Thr Tyr Ala Ala
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Thr Val Leu Gly His Ser Thr Pro Thr Ala Val Arg Pro Glu Arg Ala
1505 1510 1515 1520

Phe Arg Asp Leu Gly Phe Val Ser Val Ser Ala Val Glu Leu Arg Asn
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Arg Leu Asn Ala Val Thr Gly Leu Leu Leu Pro Thr Thr Leu Ile Phe
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Asp Tyr Pro Thr Pro Ser Ala Leu Ala Gly Tyr Leu Lys Glu Gln Leu
1555 1560 1565

Glu Glu Gly Ala Gly Gly Gln Arg Asp Ile Ala Pro Pro Val Pro Ala
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Ser Arg Val Asp Val Asp Glu Pro Ile Ala Ile Val Gly Met Ala Cys
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Arg Phe Pro Gly Gly Val Glu Ser Ala Glu Asp Leu Trp Glu Leu Val
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Ala Ser Gly Arg Asp Ala Val Gly Glu Phe Pro Val Asp Arg Gly Trp
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Asp Val Glu Ala Phe Tyr Asp Pro Glu Pro Gly Arg Ala Gly Ser Ser
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Tyr Thr Arg Arg Gly Gly Phe Leu Glu Gly Ala Ala Glu Phe Asp Ala
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Gly Phe Phe Gly Ile Ser Pro Arg Glu Ala Leu Ala Met Asp Pro Gln
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Gln Arg Leu Met Leu Glu Val Ser Trp Glu Ala Leu Glu Arg Ala Gly
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Ile Asp Pro Ala Thr Leu Arg Gly Ser Thr Thr Gly Val Phe Ala Gly
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Met Cys Ser Gln Asp Tyr Ala Asp Leu Val Arg Arg Ala Thr Glu Asp
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Leu Glu Gly Tyr Ala Met Thr Gly Leu Ser Ser Ser Val Thr Ser Gly
1730 1735 1740

Arg Val Ala Tyr Thr Leu Gly Leu Glu Gly Pro Ala Val Thr Val Asp
1745 1750 1755 1760

Thr Ala Cys Ser Ser Ser Leu Val Ala Leu His Leu Ala Cys Gln Ala
1765 1770 1775

Leu Arg Ser Gly Glu Cys Ser Leu Ala Leu Ala Gly Gly Val Thr Val
1780 1785 1790

Met Ser Thr Pro Gly Ala Phe Val Glu Phe Ser Arg Gln Arg Gly Leu
1795 1800 1805

Ser Pro Asp Gly Arg Cys Lys Ala Tyr Gly Ser Gly Ala Asp Gly Val
1810 1815 1820

Gly Trp Ala Glu Gly Val Gly Val Leu Leu Val Glu Arg Leu Ser Glu
1825 1830 1835 1840

Ala Glu Arg Arg Gly His Arg Val Leu Ala Val Val Arg Gly Ser Ala
1845 1850 1855

Val Asn Gln Asp Gly Ala Ser Asn Gly Leu Thr Ala Pro Asn Gly Pro
1860 1865 1870

Ser Gln Gln Arg Val Ile Arg Gln Ala Leu Ala Cys Ala Gly Leu Ser
1875 1880 1885

Val Ala Asp Val Asp Val Val Glu Gly His Gly Thr Gly Thr Thr Leu
1890 1895 1900

Gly Asp Pro Ile Glu Ala Gln Ala Leu Leu Ala Thr Tyr Gly Gln Gly
1905 1910 1915 1920

Arg Ser Gly Glu Arg Pro Val Trp Leu Gly Ser Val Lys Ser Asn Ile
1925 1930 1935

Gly His Ala Gln Ala Ala Ala Gly Val Ala Gly Val Ile Lys Met Val
1940 1945 1950

Met Ala Leu Arg Ala Gly Val Leu Pro Arg Thr Leu His Val Asp Glu
1955 1960 1965

Pro Ser Ser Gln Val Asp Trp Ser Ser Gly Ser Val Arg Val Leu Ala
1970 1975 1980

Asp Glu Val Glu Trp Pro Gly Val Glu Gly Arg Leu Arg Arg Ala Gly
1985 1990 1995 2000

Val Ser Ala Phe Gly Val Ser Gly Thr Asn Ala His Val Ile Leu Glu
2005 2010 2015

Glu Ala Ser Gly Gly Ala Asp Gly Gly Ala Gly Arg Leu Gln Glu Leu
2020 2025 2030

Gly Pro Gly Val Val Ser Gly Ser Gly Val Val Pro Trp Val Val Ser
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Ala Arg Ser Glu Leu Ala Leu Arg Gly Gln Ala Arg Arg Leu Arg Gly
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Val Val Ala Val Gly Gly Gly Ala Asp Gly Val Gly Val Ser Pro Ala
2065 2070 2075 2080

Gly Val Gly Arg Ala Leu Val Ser Glu Arg Ser Val Phe Glu His Arg
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Ala Val Val Val Ala Glu Asp Arg Asp Glu Phe Leu His Ala Leu Asp
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Ala Leu Ala Glu Gly Ala Pro Thr Ala Gly Val Val Gln Gly Val Ala
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Gly Pro Ala Ala Asp Gly Lys Ile Ala Met Leu Phe Gly Gly Gln Gly
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Thr His Trp Glu Gly Met Ala Gln Glu Leu Leu Gly Ser Ser Pro Val
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Phe Ala Gln Gln Met Ser Asp Cys Ala Gln Ala Leu Glu Pro Tyr Leu
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Asp Trp Ser Leu Leu Asp Val Leu Arg Gly Ala Pro Asp Ala Pro Pro
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Leu Gln Arg Val Asp Val Val Gln Pro Val Leu Phe Ala Val Met Val
2195 2200 2205

Ser Leu Ala Ala Leu Trp Arg Ser Tyr Gly Val His Pro Asp Ala Val
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Ala Gly His Ser Gln Gly Glu Ile Ala Ala Ala Tyr Val Ala Gly Ala
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Leu Ala Ala Leu Ala Gly Gln Gly Ala Met Ala Ser Val Gly Leu Pro
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Val Glu Lys Leu Glu Pro Arg Leu Ala Thr Trp Gly Asp Arg Leu Val
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Ile Ala Ala Val Asn Gly Ala Arg Ser Ala Val Val Ser Gly Glu Pro
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2355 2360 2365

Gly Thr Glu Leu Asp Ala Asp Tyr Trp Tyr Arg Asn Leu Arg Gln Val
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Glu Thr Leu Asp Glu Met Gly Asp Leu Asp Ser Leu Val Val Gly Ser
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Glu Leu Phe Val Gly Gly Val Ala Val Glu Trp Ser Gly Val Phe Gly
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Ser Val Gly Arg Gly Val Ala Gly Gly Cys Gly Val Glu Leu Pro Thr
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Tyr Ala Phe Glu Arg Glu Arg Phe Trp Leu Asp Val Glu Gly Ala Pro
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Arg Gly Ser Gly Val Ser Gly Gln Trp Gly Gly Gln Leu Ser Glu Ala
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Val Asp Thr Val Arg Gly Gly Met Leu Arg Asp Cys Leu Ala Gly Leu
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Asp Pro Ala Ala Gln Ala Glu Thr Val Leu Asp Leu Val Leu Thr His
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Ala Ala Ala Val Leu Gly His Gly Thr Ala Asp Ala Val Val Pro Glu
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Arg Ala Phe Arg Asp Leu Gly Phe Asp Ser Leu Thr Ala Val Glu Leu
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Arg Asn Arg Leu Asn Thr Ala Thr Gly Leu Arg Phe Pro Arg Thr Leu
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Val Phe Asp His Pro Arg Pro Val Ala Leu Ala Ala His Ile His Glu
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Gln Leu Ser Gly Gly Ser Pro Thr Thr Gly Thr Ala Leu Ala Leu Ala
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Leu Arg Ala Pro Ala Pro Arg Val Asp Val Asp Glu Pro Ile Ala Ile
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Val Gly Met Ala Cys Arg Phe Pro Gly Gly Val Glu Ser Ala Glu Asp
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Val Asp Arg Gly Trp Asp Val Glu Ala Phe Tyr Asp Pro Glu Pro Gly
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Ala Met Asp Pro Gln Gln Arg Leu Met Leu Glu Val Ser Trp Glu Ala
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Leu Glu Arg Ala Gly Ile Asp Pro Ala Thr Leu His Gly Ser Thr Thr
2740 2745 2750

Gly Val Phe Ala Gly Val Ser Gln Gln Asp Tyr Ala Glu Leu Leu Arg
2755 2760 2765

Arg Gly Thr Gln Asp His Glu Gly Tyr Ala Leu Thr Gly Val Ser Asn
2770 2775 2780

Ser Val Val Ser Gly Arg Leu Ser Tyr Thr Phe Gly Phe Glu Gly Pro
2785 2790 2795 2800

Ala Val Thr Val Asp Thr Ala Cys Ser Ser Ser Leu Val Ala Leu His
2805 2810 2815

Leu Ala Cys Gln Ala Leu Arg Ser Gly Glu Cys Ser Leu Ala Leu Ala
2820 2825 2830

Gly Gly Val Thr Val Met Ser Thr Pro Gly Ala Phe Val Glu Phe Ser
2835 2840 2845

Arg Gln Arg Gly Leu Ser Pro Asp Gly Arg Cys Lys Ala Tyr Gly Ser
2850 2855 2860

Gly Ala Asp Gly Val Gly Trp Ala Glu Gly Val Gly Val Leu Leu Val
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Glu Arg Leu Ser Glu Ala Glu Arg Arg Gly His Arg Val Leu Ala Val
2885 2890 2895

Val Arg Gly Ser Ala Val Asn Gln Asp Gly Ala Ser Asn Gly Leu Thr
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Ala Pro Asn Gly Pro Ser Gln Gln Arg Val Ile Arg Gln Ala Leu Ala
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Cys Ala Gly Leu Ser Val Ala Asp Val Asp Val Val Glu Gly His Gly
2930 2935 2940

Thr Gly Thr Thr Leu Gly Asp Pro Ile Glu Ala Gln Ala Leu Leu Ala
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Thr Tyr Gly Gln Gly Arg Ser Gly Glu Arg Pro Val Trp Leu Gly Ser
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Val Lys Ser Asn Ile Gly His Ala Gln Ala Ala Ala Gly Val Ala Gly
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Val Ile Lys Met Val Met Ala Leu Asn His Glu Leu Leu Pro Thr Ser
2995 3000 3005

Leu His Ile Asp Glu Pro Ser Pro His Ile Asp Trp Ser Ser Gly Gly
3010 3015 3020

Val Arg Leu Leu Thr Glu Pro Val Pro Trp Gln Gln Asn Gly Arg Pro
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Arg Arg Ala Gly Val Ser Ala Phe Gly Val Ser Gly Thr Asn Ala His
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Val Ile Ile Glu Gln Ala Pro Val Glu Ala His Val Ile Ser Glu Pro
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Val Pro Ala Glu Ala His Val Ile Val Glu Gln Ala Pro Val Glu Ala
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Pro His Val Val Asp Ala Thr Gly Pro Ala Asp Leu Thr Glu Pro Gln
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Glu Glu Ala Ala Glu Pro Glu Cys Val Ala Asp Ala Val Thr Glu Met
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Ser Ala Glu Pro Glu Cys Val Ala Asp Ala Met Ser Glu Met Ser Ala
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Glu Cys Val Ala Glu Ala Val Ser Asp Lys Ser Ala Glu Pro Glu Cys
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Val Ala Asp Ala Met Ser Asp Lys Pro Ala Leu Leu Pro Ile Pro Trp
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Leu Leu Ser Ala Lys Ser Glu Arg Ala Leu Arg Gly Gln Ala Arg Arg
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Leu Arg Gln Phe Ala Ala Arg Ala Ser Asp Ala Arg Pro Ala Asp Val
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Val Val Ala Glu Asp Arg Asp Gly Phe Leu Gln Ala Leu Asp Ala Leu
3220 3225 3230

Ala Glu Gly Arg Ser Ala Asp Gly Leu Ile Glu Gly Ser Val Gly Pro
3235 3240 3245

Arg Gly Gly His Ser Gly Arg Arg Arg Gly Lys Thr Ala Met Leu Phe
3250 3255 3260

Ala Gly Gln Gly Thr Gln Arg Val Gly Met Gly Arg Gln Leu Tyr Ala
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Ala His Pro Ala Tyr Ala Asp Ala Leu Asp Gln Val Leu Ala Glu Leu
3285 3290 3295

Asp Gly His Leu Asp Gln Pro Leu Arg Pro Leu Ile His Ala Ser Ala
3300 3305 3310

Asp Leu Ala Asp Val Ala Asp Ala Ala Asp Val Leu Asp Arg Thr Arg
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Tyr Ala Gln Pro Ala Leu Phe Ala Val Gln Val Ala Leu Phe Arg His
3330 3335 3340

Leu Glu Arg Leu Gly Val Arg Ala Asp Phe Val Ala Gly His Ser Ile
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Gly Glu Leu Ala Ala Ala His Val Ala Gly Val Leu Pro Leu Ala Ala
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Pro Gly Gly Ala Met Val Ala Val Arg Ala Ser Glu Ala Glu Ala Arg
3395 3400 3405

Gln Ala Leu Asp Gly Arg Glu Ala Arg Val Ser Val Ala Ala Val Asn
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Gly Pro Ala Ser Val Val Phe Ser Gly Ala Glu Asp Glu Val Gly Asn
3425 3430 3435 3440

Met Ala Asp Trp Phe Ala Glu Arg Gly Arg Arg Val Lys Arg Leu Arg
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Thr Gly His Ala Phe His Ser Pro Leu Met Asp Pro Met Leu Glu Glu
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Phe Gln Gln Val Ala Ala Ser Leu Thr Tyr Ser Glu Pro Ala Ile Pro
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Met Val Ser Thr Leu Thr Gly Asp Ile Val Ala Ala Gly Glu Leu Ser
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Asp Pro Glu Tyr Trp Val Arg Gln Val Arg Arg Thr Val Arg Phe Gly
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Asp Ala Ile Ser Arg Leu His Thr Asp Gly Val Arg Thr Phe Met Glu
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Leu Gly Pro Asp Gly Thr Leu Ser Ala Leu Ala Glu Glu Cys Leu Glu
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Glu Asn Leu Leu Ile Pro Leu Leu Arg Pro Asp Ser Pro Glu Pro Gly
3570 3575 3580

Thr Leu Leu Thr Gly Leu Ala Arg Leu His Thr His Gly Ala Ala Ala
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Val Asn Trp Pro Ala Ala Leu Pro Glu Arg Asp Arg Ala Arg His Leu
3605 3610 3615

Asp Leu Pro Thr Tyr Ala Phe Asp His His Arg Tyr Trp Val Asp Thr
3620 3625 3630

Ser Ala Gly His Pro Gly Asp Leu Ser Ala Ala Gly Leu Gly Thr Ala
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Gly His Pro Leu Leu Gly Ser Ala Val Ala Leu Ala Glu Ser Gln Glu
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Leu Leu Phe Thr Gly Arg Leu Ser Leu Arg Thr His Pro Trp Leu Ala
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Asp His Ala Ile Phe Gly Thr Val Leu Leu Pro Gly Thr Ala Ile Leu
3685 3690 3695

Glu Leu Ala Val Arg Ala Gly Asp Glu Val Asp Cys Gly Thr Val Glu
3700 3705 3710

Glu Leu Thr Leu Arg Thr Pro Leu Val Leu Pro Glu Gln Gly Ser Val
3715 3720 3725

Ile Leu Gln Leu Ser Val Gly Ala Pro Gln Gly Pro Gln Thr Pro Glu
3730 3735 3740

Glu Pro Glu Arg Arg Thr Phe Ala Leu Tyr Ala Arg Glu Asp Asp Gly
3745 3750 3755 3760

Leu Ser Ser Ser Ser Ala Ala Ala Thr Gly Thr Glu Trp Thr Cys His
3765 3770 3775

Ala Thr Gly Val Leu Thr Gly Thr Ala Arg Pro Ala Glu Glu His Thr
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Gln Glu Pro Trp Pro Pro Ala Asp Ala Ala Pro Val Asp Leu Asp Gly
3795 3800 3805

Trp Tyr Glu Gln Leu Ala Gly Ala Gly Leu Gly Tyr Gly Pro Val Phe
3810 3815 3820

Gln Gly Leu Arg Glu Val Trp Arg Arg Gly Asp Glu Val Phe Ala Val
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Val Thr Leu Pro Glu Ser Thr Glu Gly Gln Ala Ala Asp Ala Ala Arg
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Tyr Ala Leu His Pro Ala Leu Leu Asp Ala Ala Leu His Pro Val Val
3860 3865 3870

Leu Arg His Glu Gly Asp Ala Ala Ala Asp Gly His Gly Trp Leu Pro
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Phe Ser Trp Thr Gly Val Thr Val Ala Ala Ser Gly Ala Ser Thr Leu
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His Val Arg Leu Thr Val Arg Thr Asp Glu Asp Ala Val Gly Leu Leu
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His Asp His Leu Phe Arg Ile Glu Trp Arg Pro Leu His Leu Pro Thr
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Arg Thr Ala Ala Val Leu Glu Arg Asn Gly Ala Ser Trp Gln Ala Tyr
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Pro Gly Met Val Val Ile Ser Cys Glu Pro Asp Gly Ala Ser Ala Pro
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Thr Arg Asp Ala Gly Leu Thr Thr Phe Thr Val Phe Ser Ser Ala Ala
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Arg Ser Leu Ala Trp Gly Leu Trp Gly Glu Ala Asp Gly Met Thr Arg
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Pro Leu Ser Asn Ala Gln Gly Leu Ala Leu Leu Asp Thr Ala Asp Arg
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His Gly Leu Ile Arg Ile Pro Ala Arg Arg Ser Ala Asp His Gly Ile
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Cys Leu Pro Thr Val Ala Ala Val Ser Ser Val Tyr Gln Tyr Ser Arg
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Thr Ser His Leu Glu Arg Leu Gly Val Arg Pro Glu Ala Val Val Thr
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Met Glu Ala Ser Ser Glu Pro Ile Ala Ile Val Gly Met Ala Cys Arg
35 40 45

Phe Pro Gly Gly Val Cys Ser Pro Glu Glu Leu Trp Glu Leu Val Ala
50 55 60

Ser Gly Gly Asp Ala Ile Gly Glu Phe Pro Ala Gly Arg Gly Trp Asp
65 70 75 80

Leu Glu Gly Leu Phe Asp Ser Asp Pro Asp Arg Ser Gly Thr Ser Tyr
85 90 95

Ala Arg Tyr Gly Gly Phe Leu Tyr Glu Ala Gly Glu Phe Asp Ala Asp
100 105 110

Phe Phe Gly Ile Ser Pro Arg Glu Ala Leu Ala Met Asp Pro Gln Gln
115 120 125

Arg Leu Leu Leu Glu Thr Ser Trp Glu Ala Phe Glu Arg Ala Gly Ile
130 135 140

Asp Pro Leu Ser Met Arg Gly Ser Arg Thr Gly Val Phe Ala Gly Val
145 150 155 160

Met Tyr His Asp Tyr Gly Ser Arg Leu Gly Thr Ile Pro Glu Gly Phe
165 170 175

Glu Gly Tyr Ile Gly Asn Gly Ser Gly Gly Ala Val Ala Ser Gly Arg
180 185 190

Val Ala Tyr Thr Leu Gly Leu Glu Gly Pro Ala Val Ser Val Asp Thr
195 200 205

Ala Cys Ser Ser Ser Leu Val Ala Leu His Leu Ala Cys Gln Ser Leu
210 215 220

Arg Ser Gly Glu Cys Thr Leu Ala Leu Ala Gly Gly Val Thr Val Met
225 230 235 240

Ser Thr Pro His Leu Phe Val Glu Phe Ser Arg Gln Arg Gly Leu Ser
245 250 255

Val Asp Gly Arg Cys Lys Ser Phe Ala Gly Gly Ala Asp Gly Thr Gly
260 265 270

Met Gly Glu Gly Val Gly Met Leu Leu Val Glu Arg Leu Ser Asp Ala
275 280 285

Val Arg Leu Gly His Arg Val Leu Ala Val Leu Arg Gly Ser Ala Val
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Asn Gln Asp Gly Ala Ser Asn Gly Leu Thr Ala Pro Asn Gly Pro Ala
305 310 315 320

Gln Glu Arg Val Ile Arg Gln Ala Leu Ala Asn Ala Gly Leu Ser Val
325 330 335

Ala Asp Val Asp Val Val Glu Gly His Gly Thr Gly Thr Thr Leu Gly
340 345 350

Asp Pro Ile Glu Ala Gln Ala Leu Leu Ala Thr Tyr Gly Gln Arg Ala
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Gly Asn Arg Pro Leu Trp Leu Gly Ser Val Lys Ser Asn Ile Gly His
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Ala Gln Ala Ala Ala Gly Val Gly Gly Val Ile Lys Met Val Met Ala
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Leu Arg Glu Gly Val Leu Pro Arg Thr Leu His Val Asp Glu Pro Ser
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Pro Gln Val Asp Trp Ser Ala Gly Ala Val Arg Leu Leu Thr Glu Ala
420 425 430

Val Pro Trp Pro Gly Asp Ala Ala Gly Arg Leu Arg Arg Ala Gly Val
435 440 445

Ser Ser Phe Gly Val Ser Gly Thr Asn Ala His Val Ile Leu Glu Glu
450 455 460

Ala Pro Ala Ala Gly Gly Cys Val Ala Gly Gly Gly Val Leu Glu Gly
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Ala Pro Gly Leu Ala Ile Ser Val Ala Glu Ser Val Ala Ala Pro Val
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Ala Val Ser Ala Pro Val Ala Glu Ser Val Pro Val Pro Val Pro Val
500 505 510

Pro Val Pro Val Pro Val Ser Ala Arg Ser Glu Ala Gly Leu Arg Ala
515 520 525

Gln Ala Glu Ala Leu Arg Gln Tyr Val Ala Val Arg Pro Asp Val Ser
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Leu Ala Asp Val Gly Ala Gly Leu Ala Cys Gly Arg Ala Val Leu Glu
545 550 555 560

His Arg Ala Val Val Leu Ala Ala Asp Arg Glu Glu Leu Val Gln Gly
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Leu Gly Ala Leu Ala Ala Gly Glu Pro Asp Arg Arg Val Thr Thr Gly
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His Ala Pro Gly Gly Asp Arg Gly Gly Val Val Phe Val Phe Pro Gly
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Gln Gly Gly Gln Trp Ala Gly Met Gly Val Arg Leu Leu Ala Ser Ser
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Pro Val Phe Ala Arg Arg Met Gln Ala Cys Glu Glu Ala Leu Ala Pro
625 630 635 640

Trp Val Asp Trp Ser Val Val Asp Ile Leu Arg Arg Asp Ala Gly Asp
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Ala Val Trp Glu Arg Ala Asp Val Val Gln Pro Val Leu Phe Ser Val
660 665 670

Met Val Ser Leu Ala Ala Leu Trp Arg Ser Tyr Gly Ile Glu Pro Asp
675 680 685

Ala Val Leu Gly His Ser Gln Gly Glu Ile Ala Ala Ala His Val Cys
690 695 700

Gly Ala Leu Ser Leu Lys Asp Ala Ala Lys Thr Val Ala Leu Arg Ser
705 710 715 720

Arg Ala Leu Ala Ala Val Arg Gly Arg Gly Gly Met Ala Ser Val Pro
725 730 735

Leu Pro Ala Gln Glu Val Glu Gln Leu Ile Gly Glu Arg Trp Ala Gly
740 745 750

Arg Leu Trp Val Ala Ala Val Asn Gly Pro Arg Ser Thr Ala Val Ser
755 760 765

Gly Asp Ala Glu Ala Val Asp Glu Val Leu Ala Tyr Cys Ala Gly Thr
770 775 780

Gly Val Arg Ala Arg Arg Ile Pro Val Asp Tyr Ala Ser His Cys Pro
785 790 795 800

His Val Gln Pro Leu Arg Glu Glu Leu Leu Glu Leu Leu Gly Asp Ile
805 810 815

Ser Pro Gln Pro Ser Gly Val Pro Phe Phe Ser Thr Val Glu Gly Thr
820 825 830

Trp Leu Asp Thr Thr Thr Leu Asp Ala Ala Tyr Trp Tyr Arg Asn Leu
835 840 845

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850 855 860

Gly His Arg Val Phe Val Glu Val Ser Pro His Pro Thr Leu Val Pro
865 870 875 880

Ala Ile Glu Asp Thr Thr Glu Asp Thr Ala Glu Asp Val Thr Ala Ile
885 890 895

Gly Ser Leu Arg Arg Gly Asp Asn Asp Thr Arg Arg Phe Leu Thr Ala
900 905 910

Leu Ala His Thr His Thr Thr Gly Ile Gly Thr Pro Thr Thr Trp His
915 920 925

His His Tyr Thr His His His Thr His Pro His Asn His His Leu Asp
930 935 940

Leu Pro Thr Tyr Pro Phe Gln Arg Gln His Tyr Trp Leu Asp Ala Pro
945 950 955 960

Thr Gly Ala Gly Asp Val Ala Ala Ala Gly Leu Glu Pro Ala Glu His
965 970 975

Pro Leu Leu Ala Ala Thr Val Gln Leu Ala Asp Thr Asp Gly Cys Leu
980 985 990

Leu Thr Gly Arg Leu Ser Leu Arg Ser His Pro Trp Leu Gly Asp Tyr
995 1000 1005

Glu Val Gly Gly Ala Val Leu Leu Ser Gly Ser Ala Phe Val Glu Leu
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Gly Ala Asp Asn Gly Ala Gln Leu His Ala Arg Leu Ala Gly Gln Thr
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His Glu Gln Gln His Thr Thr Leu Leu Ala Leu Val Arg Ser His Ile
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Asn Arg Leu Ser Arg Thr Thr Gly Leu Arg Leu Pro Thr Thr Leu Ala
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Phe Asp His Pro Asn Pro Thr Thr Leu Thr His His Leu His Thr Gln
1825 1830 1835 1840

Leu Leu Gly Ser Asp Ser Thr Ala Ser Ile Pro Ala Pro Arg Ala Ala
1845 1850 1855

Ala Val Pro Ala Asp Gln Asp Glu Pro Val Ala Ile Ile Gly Met Ala
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Cys Arg Tyr Pro Gly Gly Val Thr Ser Ala Glu Glu Leu Trp Glu Leu
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Trp Asp Leu Glu Ala Leu Phe Asp Pro Glu Pro Gly Arg Pro Gly Thr
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1955 1960 1965

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Gly Thr Val Phe Ala Ala Lys Val Asp Ala Ala Leu Leu Leu Asp Glu
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gga ctc gac ccc acc gaa cac ccc cta ctc ggc gcc aca ttg gaa ctg   96
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gcg act gac ggt gga gcg ctt ctt gca ggg cgc ttg tct ttg agg tcg   144
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cat ccg tgg ctg gct gac tac gag gtc ggc ggc acg gtg ctg ctg tcg   192
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ggc gcc acc ttc ctc gaa ctc gcc ctt cat gcg ggc aca tac gtg ggc   240
Gly Ala Thr Phe Leu Glu Leu Ala Leu His Ala Gly Thr Tyr Val Gly
 65                  70                  75                  80

tgc gac cga gtg gat gag ctg acg ctg cat gcg ccg ctg gtg gtt cct   288
Cys Asp Arg Val Asp Glu Leu Thr Leu His Ala Pro Leu Val Val Pro
                 85                  90                  95

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gag ggg cgg cgt ttg gtg agt gtg tat gcg cgg ggt ggg agt gct tgt   384
Glu Gly Arg Arg Leu Val Ser Val Tyr Ala Arg Gly Gly Ser Ala Cys
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ggt ggg ggt ggt gcg tcg ggt ggg gtg tgg acg tgt cat gcc tcg ggg   432
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09/529,185 PCT/US98/20950

09/914286
518 Rec'd PCT/PTO 24 AUG 2001

SPECIFICATION

2/pats

Avermectin Aglycon Synthase Genes

Technical Field

The present invention relates to DNAs encoding multifunctional enzyme involved in the biosynthesis of an avermectin compound which is a polyketide; polypeptides encoded by the DNAs; vectors containing the DNAs; host cells transformed with the DNAs or the vectors; and a process for producing avermectin.

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Background Art

A polyketide is a group of compounds containing a number of natural substances which vary in their structures and functions. Polyketides are known to include compounds having a variety of bioactivities such as antibacterial agents, antimyotic agents, antiparasitic agents, anti-insect agents, antitumor agents, and immunosuppressant agents, and aromatic compounds which are produced by bacteria, fungi and plants.

The above-mentioned various polyketide compounds are synthesized by the same biosynthetic mechanism which is very similar to the biosynthesis of fatty acids. That is, a polyketide compound is biosynthesized by the steps of continuous condensation of lower fatty acids including acetic acids and propionic acids, and subsequent reactions such as reduction of ketone, dehydration and enoyl reduction of each carbonyl group at β position of the extended acyl group which is similar to fatty acid synthesis. These various repetitive synthetic processes of many polyketide compounds are carried out a macromolecule, multifunctional enzyme complex, which has specific active sites (domains) required for each catalytic activity. A general reaction manner of polyketide biosynthesis is outlined, for example in Ann. Rev. Gen., 24, 37 (1990), and Ann. Rev. Microbiol., 47, 875 (1993).

It has been shown that a DNA sequence encoding polyketide synthase usually encodes all the required activities for the synthesis of a polyketide backbone. The DNA sequence encoding polyketide synthase is composed of modules, that is, repeating units involving condensation steps and modification steps following condensation. Each catalytic activity is involved in specificity to a specific carboxylic acid component of each condensation step, or in a different site which specifies a modification function following a specific condensation step to be achieved. For example, International Publication WO93/13663 describes the constitution of a gene encoding polyketide synthase of *Saccharopolyspora erythaea*. This gene consists of 6 modules, each of which is responsible for one condensation step. That is, a correct sequence of acyl side chain elongation and modification of an elongating chain are determined by genetic information present in each module.

Regarding the biosynthetic mechanism of avermectin aglycon, it has been reported that like other polyketide compounds, synthesis units of avermectin aglycon are lower fatty acids, such as acetic acid and propionic acid as its components [J. Antibiot., 39, 541-549 (1986)], and as in *Saccharopolyspora erythaea*, polyketide synthase consisting of modules is present in avermectin-producing bacteria [Gene, 115, 119-125 (1992), Ann. New York Acad. of Sci., 721, 123-132 (1994)].

Japanese Published Unexamined Patent Application No. 15391/91 describes a DNA fragment involved in avermectin biosynthesis, but shows no nucleotide sequence of the DNA fragment. This publication merely assumes the presence of polyketide synthase, which is involved in the synthesis of avermectin aglycon and the presence of partial modules. Therefore, the entire structure of polyketide synthase of avermectin cannot be predicted.

Similarly, MacNeil et al have reported a domain structure of partial modules

[Ann. New York Acad. of Sci., 721, 123-132 (1994)]. However, they have not revealed the nucleotide sequence that should be evidence for polyketide synthase of avermectin.

Alteration of polyketide synthase would be a very useful breeding technique upon breeding of bacterial strains which can be used for a novel process for producing a novel avermectin useful as veterinary drugs and agricultural chemicals, and can produce a more effective avermectin derivative. Steps required to carry out such alteration include determination of the entire nucleotide sequence of a gene encoding polyketide synthase, accurate determination of a domain structure of each module based on the sequence, and introduction of a desired mutation. However, as described above, it was very difficult to carry out such improved-breeding, since the polyketide synthase gene of avermectin aglycon had not been specified and the nucleotide sequence of the gene was unknown.

The present inventors have studied approaches for producing a component different from that produced by the wild type strain by engineering DNA involved in polyketide synthesis with various methods. To apply this methodology, first we had to isolate a DNA molecule involved in the biosynthesis of a polyketide compound.

Hence, an object of the present invention is to provide a DNA encoding a multifunctional enzyme involved in biosynthesis of avermectin aglycon, and a process for producing avermectin aglycon, altered avermectin aglycon, avermectin, and altered avermectin using the DNA.

Disclosure of the Invention

The present inventors made an intensive investigation to attain the object. As a result, the inventors have succeeded in isolating DNAs encoding a multifunctional enzyme involved in biosynthesis of avermectin aglycon. The present invention has

been completed on the basis of this result.

The present invention relates to the following (1) to (43).

(1) A DNA encoding avermectin aglycon synthase (hereinafter, also referred to as an avermectin aglycon synthase gene).

In an embodiment of the present invention, the DNA is derived from a wild-type avermectin-producing strain or a mutant strain thereof, such as one belonging to the genus *Streptomyces*, specifically *Streptomyces avermitilis*.

(2) A DNA comprising a nucleotide sequence selected from the group consisting of nucleotide Nos. 1-11916 and 11971-30688 of SEQ ID NO: 1, and nucleotide Nos. 1-14643 and 14824-31419 of SEQ ID NO: 2; or
a DNA which hybridizes with this DNA under stringent conditions and which encodes a polypeptide having avermectin aglycon synthase activity.

The above term "a DNA which hybridizes with this DNA under stringent conditions" refers to a DNA which is obtained by colony hybridization, plaque hybridization or Southern hybridization or the like using the DNA having a nucleotide sequence of SEQ ID NO. 1 or 2. For example, such a DNA can be identified by carrying out hybridization at 65°C in the presence of 0.7 to 1.0 mol/l sodium chloride using a filter on which DNAs derived from colonies or plaques have been immobilized, followed by washing the filter at 65℃ using 0.1 to 2-fold concentrated SSC solution (1-fold concentrated SSC solution consists of 150 mmol/l sodium chloride, 15 mmol/l sodium citrate).

Hybridization can be carried out according to a method described in experimental protocols, such as Molecular Cloning, A Laboratory Manual, Second Edition, Cold Spring Harbor Laboratory Press, 1989 (hereinafter abbreviated as

Molecular Cloning 2nd Edition), Current Protocols in Molecular Biology, John Wiley & Sons, 1987-1997 (hereinafter abbreviated as Current Protocols in Molecular Biology), DNA Cloning 1; Core Techniques, A Practical Approach, Second Edition, Oxford University, 1995. Specific examples of the DNA which can be hybridized include a DNA having at least homology of 80% or more, preferably 95% or more with a nucleotide sequence selected from the group consisting of nucleotide Nos. 1-11916 and 11971-30688 of SEQ ID NO: 1, and nucleotide Nos. 1-14643 and 14824-31419 of SEQ ID NO: 2.

The following term "a DNA which hybridizes with this DNA (or said DNA) under stringent conditions" can also be defined in the same manner as described above.

(3) The DNA according to the above (1) or (2) wherein the DNA comprises DNAs encoding avermectin aglycon synthase domains.

(4) The DNA according to the above (3) wherein the DNA encoding avermectin aglycon synthase domains is selected from the group consisting of:

a DNA encoding a polypeptide having acyltransferase activity and acyl carrier protein activity;

a DNA encoding a polypeptide having β-ketoacyl-ACP synthase activity, acyltransferase activity, β-ketoacyl-ACP reductase activity and acyl carrier protein activity;

a DNA encoding a polypeptide having β-ketoacyl-ACP synthase activity, acyltransferase activity, dehydratase activity, β-ketoacyl-ACP reductase activity and acyl carrier protein activity;

a DNA encoding a polypeptide having β-ketoacyl-ACP synthase activity, acyltransferase activity, and acyl carrier protein activity; and

a DNA encoding a polypeptide having β-ketoacyl-ACP synthase activity, acyltransferase activity, dehydratase activity, β-ketoacyl-ACP reductase activity, acyl

carrier protein activity, and thioesterase activity.

(5) The DNA according to the above (4) wherein the DNA encoding a polypeptide having acyltransferase activity and acyl carrier protein activity is a DNA comprising the nucleotide sequence of nucleotide Nos. 85-1353 of SEQ ID NO: 1; or
a DNA which hybridizes with this DNA under stringent conditions and which encodes a polypeptide having acyltransferase activity and acyl carrier protein activity.

(6) The DNA according to the above (4) wherein the DNA encoding a polypeptide having β-ketoacyl-ACP synthase activity, acyltransferase activity, β-ketoacyl-ACP reductase activity, and acyl carrier protein activity is:
a DNA comprising the nucleotide sequence selected from the group consisting of nucleotide Nos. 1441-6180, 15217-19938 and 20008-24690 of SEQ ID NO: 1, and nucleotide Nos. 100-4692 and 14935-20334 of SEQ ID NO: 2; or
a DNA which hybridizes with this DNA under stringent conditions and which encodes a polypeptide having β-ketoacyl-ACP synthase activity, acyltransferase activity, β-ketoacyl-ACP reductase activity, and acyl carrier protein activity.

(7) The DNA according to the above (4) wherein the DNA encoding a polypeptide having β-ketoacyl-ACP synthase activity, acyltransferase activity, dehydratase activity, β-ketoacyl-ACP reductase activity, and acyl carrier protein activity is:
a DNA comprising the nucleotide sequence selected from the group consisting of nucleotide Nos. 6256-11658 and 24781-30309 of SEQ ID NO: 1, and nucleotide Nos. 20413-25734 and 25810-31125 of SEQ ID NO: 2; or
a DNA which hybridizes with this DNA under stringent conditions and which encodes polypeptides having β-ketoacyl-ACP synthase activity, acyltransferase activity, dehydratase activity, β-ketoacyl-ACP reductase activity, and acyl carrier protein activity.

(8) The DNA according to the above (4) wherein the DNA encoding a polypeptide having β-ketoacyl-ACP synthase activity, acyltransferase activity, and acyl carrier protein activity is:

a DNA comprising the nucleotide sequence of nucleotide No. 12076-15147 of SEQ ID NO: 1, or nucleotide No. 4771-7818 of SEQ ID NO: 2;

or a DNA which hybridizes with this DNA under stringent conditions and which encodes a polypeptide having β-ketoacyl-ACP synthase activity, acyltransferase activity, and acyl carrier protein activity.

(9) The DNA according to the above (4) wherein the DNA encoding a polypeptide having β-ketoacyl-ACP synthase activity, acyltransferase activity, dehydratase activity, β-ketoacyl-ACP reductase activity, acyl carrier protein activity, and thioesterase activity is:

a DNA comprising the nucleotide sequence of nucleotide Nos. 7906-14619 of SEQ ID NO: 2; or

a DNA which hybridizes with this DNA under stringent conditions and which encodes a polypeptide having β-ketoacyl-ACP synthase activity, acyltransferase activity, dehydratase activity, β-ketoacyl-ACP reductase activity, acyl carrier protein activity, and thioesterase activity.

(10) The DNA according to the above (4) wherein the DNA encoding a polypeptide having acyltransferase activity is:

a DNA comprising the nucleotide sequence selected from the group consisting of nucleotide Nos. 85-1032, 7906-8829, 13756-14694, 16917-17862, 21658-22584, and 26413-27336 of SEQ ID NO: 1, and nucleotide Nos. 1648-2673, 6322-7344, 9676-10773, 16543-17565, 21991-23019 and 27367-28392 of SEQ ID NO: 2; or

a DNA which hybridizes with this DNA under stringent conditions and which encodes a polypeptide having acyltransferase activity.

(11) The DNA according to the above (4) wherein the DNA encoding a polypeptide having acyl carrier protein activity is:

a DNA comprising the nucleotide sequence selected from the group consisting of nucleotide Nos. 1096-1353, 5935-6180, 11413-11658, 14902-15147, 19693-19938, 24445-24690 and 30064-30309 of SEQ ID NO: 1, and nucleotide Nos. 4447-4692, 7573-7818, 13378-13659, 20089-20334, 25489-25734 and 30880-31125 of SEQ ID NO: 2; or

a DNA which hybridizes with this DNA under stringent conditions and which encodes a polypeptide having acyl carrier protein activity.

(12) The DNA according to the above (4) wherein the DNA encoding a polypeptide having β-ketoacyl-ACP synthase activity is:

a DNA comprising the nucleotide sequence selected from the group consisting of nucleotide Nos. 1441-2742, 6256-7545, 12076-13368, 15217-16506, 20008-21297 and 24781-26079 of SEQ ID NO: 1, and nucleotide Nos. 100-1383, 4771-6060, 7906-9258, 14935-16224, 20413-21705 and 25810-27102 of SEQ ID NO: 1; or

a DNA which hybridizes with this DNA under stringent conditions and which encodes a polypeptide having β-ketoacyl-ACP synthase activity.

(13) The DNA according to the above (4) wherein the DNA encoding a polypeptide having β-ketoacyl-ACP reductase activity is:

a DNA comprising the nucleotide sequence selected from the group consisting of nucleotide Nos. 5143-5676, 10609-11142, 18886-19419, 23602-24138 and 29227-29760 of SEQ ID NO: 1, and nucleotide Nos. 3634-4188, 12547-13104, 19285-19842, 24685-25242 and 30076-30633 of SEQ ID NO: 2; or

a DNA which hybridizes with this DNA under stringent conditions and which encodes a polypeptide having β-ketoacyl-ACP reductase activity.

(14) The DNA according to the above (4) wherein the DNA encoding a

polypeptide having dehydratase activity is:

a DNA comprising the nucleotide sequence selected from the group consisting of nucleotide Nos. 8947-9384 and 27475-27894 of SEQ ID NO: 1, and nucleotide Nos. 10885-11289, 23149-23529 and 28516-28878 of SEQ ID NO: 2; or

a DNA which hybridizes with this DNA under stringent conditions and which encodes a polypeptide having dehydratase activity.

(15) The DNA according to the above (4) wherein the DNA encoding a polypeptide having thioesterase activity is:

a DNA having the nucleotide sequence of nucleotide No. 13879-14619 of SEQ ID NO: 2; or

a DNA which hybridizes with this DNA under stringent conditions and which encodes a polypeptide having thioesterase activity.

(16) The DNA according to the above (3) or (4) wherein the DNA encoding an avermectin aglycon synthase domain is a mutated DNA encoding a polypeptide having enhanced or diminished activity of the domain.

(17) The DNA according to the above (16) wherein the DNA encoding a polypeptide having diminished activity of avermectin aglycon synthase domain is the DNA comprising a nucleotide sequence of SEQ ID NO: 7.

(18) A DNA encoding an avermectin aglycon synthase domain which comprises a nucleotide sequence selected from the group consisting of nucleotide Nos. 85-1032, 1096-1353, 1441-2742, 3148-4068, 5143-5676, 5935-6180, 6256-7545, 7906-8829, 8947-9384, 10609-11142, 11413-11658, 12076-13368, 13756-14694, 14902-15147, 15217-16506, 16917-17862, 18886-19419, 19693-19938, 20008-21297, 21658-22584, 23602-24138, 24445-24690, 24781-26079, 26413-27336, 27475-27894, 29227-29760 and 30064-30309 of SEQ ID NO: 1, and nucleotide Nos. 100-1383, 1648-2673,

3634-4188, 4447-4692, 4771-6060, 6322-7344, 7573-7818, 7906-9258, 9676-10773, 10885-11289, 12547-13104, 13378-13659, 13879-14619, 14935-16224, 16543-17565, 17689-18066, 19285-19842, 20089-20334, 20413-21705, 21991-23019, 23149-23529, 24685-25242, 25489-25734, 25810-27102, 27367-28392, 28516-28878, 30076-30633, and 30880-31125 of SEQ ID NO: 2; or

a DNA which hybridizes with this DNA under stringent conditions and which encodes a polypeptide having avermectin aglycon synthase domain activity.

(19) A DNA comprising the nucleotide sequence of nucleotide No. 85-1353 of SEQ ID NO: 1 ;or

a DNA which hybridizes with this DNA under stringent conditions and which encodes a polypeptide having acyltransferase activity and acyl carrier protein activity.

(20) A DNA comprising the nucleotide sequence selected from the group consisting of nucleotide Nos. 1441-6180, 15217-19938 and 20008-24690 of SEQ ID NO: 1, and nucleotide Nos. 100-4692 of SEQ ID NO: 2; or

a DNA which hybridizes with this DNA under stringent conditions and which encodes a polypeptide having β-ketoacyl-ACP synthase activity, acyltransferase activity, β-ketoacyl-ACP reductase activity and acyl carrier protein activity.

(21) A DNA comprising the nucleotide sequence selected from the group consisting of nucleotide Nos. 6256-11658 and 24781-30309 of SEQ ID NO: 1, and nucleotide Nos. 14935-20334, 20413-25734 and 25810-31125 of SEQ ID NO: 2; or

a DNA which hybridizes with this DNA under stringent conditions and which encodes a polypeptide having β-ketoacyl-ACP synthase activity, acyltransferase activity, dehydratase activity, β-ketoacyl-ACP reductase activity and acyl carrier protein activity.

(22) A DNA comprising the nucleotide sequence of nucleotide No. 12076-15147 of SEQ ID NO: 1, or the nucleotide sequence of nucleotide No. 4771-7818 of SEQ ID

NO: 2; or

a DNA which hybridizes with this DNA under stringent conditions and which encodes a polypeptide having β-ketoacyl-ACP synthase activity, acyltransferase activity, and acyl carrier protein activity.

(23) A DNA comprising the nucleotide sequence of nucleotide No. 7906-14619 of SEQ ID NO: 2; or

a DNA which hybridizes with this DNA under stringent conditions and which encodes a polypeptide having β-ketoacyl-ACP synthase activity, acyltransferase activity, dehydratase activity, β-ketoacyl-ACP reductase activity, acyl carrier protein activity, and thioesterase activity.

(24) A DNA comprising the nucleotide sequence selected from the group consisting of nucleotide Nos. 85-1032, 7906-8829, 13756-14694, 16917-17862, 21658-22584 and 26413-27336 of SEQ ID NO: 1, and nucleotide Nos. 1648-2673, 6322-7344, 9676-10773, 16543-17565, 21991-23019 and 27367-28392 of SEQ ID NO: 2; or

a DNA which hybridizes with this DNA under stringent conditions and which encodes a polypeptide having acyltransferase activity.

(25) A DNA comprising the nucleotide sequence selected from the group consisting of nucleotide Nos. 1096-1353, 5935-6180, 11413-11658, 14902-15147, 19693-19938, 24445-24690, and 30064-30309 of SEQ ID NO: 1, and nucleotide Nos. 4447-4692, 7573-7818, 13378-13659, 20089-20334, 25489-25734 and 30880-31125 of SEQ ID NO: 2; or

a DNA which hybridizes with this DNA under stringent conditions and which encodes a polypeptide having acyl carrier protein activity.

(26) A DNA comprising the nucleotide sequence selected from the group

consisting of nucleotide Nos. 1441-2742, 6256-7545, 12076-13368, 15217-16506, 20008-21297 and 24781-26079 of SEQ ID NO: 1, and nucleotide Nos. 100-1383, 4771-6060, 7906-9258, 14935-16224, 20413-21705, and 25810-27102 of SEQ ID NO: 1; or

a DNA which hybridizes with this DNA under stringent conditions and which encodes a polypeptide having β-ketoacyl-ACP synthase activity.

(27) A DNA comprising the nucleotide sequence selected from the group consisting of nucleotide Nos. 5143-5676, 10609-11142, 18886-19419, 23602-24138, and 29227-29760 of SEQ ID NO: 1, and nucleotide Nos. 3634-4188, 12547-13104, 19285-19842, 24685-25242 and 30076-30633 of SEQ ID NO: 2; or

a DNA which hybridizes with this DNA under stringent conditions and which encodes a polypeptide having β ketoacyl ACP reductase activity.

(28) A DNA comprising the nucleotide sequence selected from the group consisting of nucleotide Nos. 8947-9384 and 27475-27894 of SEQ ID NO: 1, and nucleotide Nos. 10885-11289, 17689-18066, 23149-23529 and 28516-28878 of SEQ ID NO: 2; or

a DNA which hybridizes with this DNA under stringent conditions and which encodes a polypeptide having dehydratase activity.

(29) A DNA comprising the nucleotide sequence of nucleotide Nos. 13879-14619 of SEQ ID NO: 2; or

a DNA which hybridizes with this DNA under stringent conditions and which encodes a polypeptide having thioesterase activity.

(30) A DNA comprising the nucleotide sequence shown in SEQ ID NO: 7.

(31) A polypeptide encoded by the DNA according to any one of the above (1) to

(29) .

(32) A polypeptide comprising the amino acid sequence according to any one of SEQ ID NOS: 3 to 6; or

a polypeptide comprising an amino acid sequence wherein one or more amino acids are deleted, replaced or added in the amino acid sequence according to any one of SEQ ID NOS: 3 to 6, and having avermectin aglycon synthase activity.

The above "polypeptide comprising an amino acid sequence wherein one or more amino acids are deleted, replaced or added, and having avermectin aglycon synthase activity" can be prepared according to site-directed mutagenesis as described in Molecular Cloning, 2nd Edition, Current Protocols in Molecular Biology, Nucleic Acids Research, 10, 6487 (1982), Proc. Natl. Acad. Sci., USA, 79, 6409 (1982), Gene, 34, 315 (1985), Nucleic Acids Research, 13, 4431 (1985), Proc. Natl. Acad. Sci USA, 82, 488 (1985) and the like. The number of amino acids which are deleted, replaced or added is not specifically limited, but is a number of amino acids which can be deleted, replaced, or added by known methods, such as the above site-directed mutagenesis, and within the range from 1 to several tens of amino acids, preferably 1 to 20, more preferably 1 to 10, and even more preferably 1 to 5 amino acids.

(33) A polypeptide comprising the amino acid sequence selected from the group consisting of amino acid Nos. 29-344, 366-451, 481-914, 1050-1356, 1715-1892, 1979-2060, 2086-2515, 2983-3128, 3537-3714 and 3805-3886 of SEQ ID NO: 3, amino acid Nos. 36-466, 596-908, 978-1059, 1083-1512, 1653-1964, 2306-2483, 2575-2656, 2680-3109, 32030-3538, 3878-4056, 4159-4240, 4271-4703, 4815-5122, 5753-5930 and 6032-6113 of SEQ ID NO: 4, amino acid Nos. 34-461, 550-891, 1212-1396, 1483-1564, 1591-2020, 2108-2448, 2525-2606, 2636-3086, 3226-3591, 3629-3763, 4183-4363, 4460-4553 and 4627-4873 of SEQ ID NO: 5, amino acid Nos. 38-467, 574-914, 956-1081, 1488-1673, 1756-1837, 1864-2294, 2390-2732, 2776-2902,

3288-3473, 3556-3637, 3663-4093, 4182-4523, 4565-4685, 5085-5270 and 5353-5434 of SEQ ID NO: 6; or

a polypeptide comprising an amino acid sequence wherein one or more amino acids are deleted, replaced or added in the amino acid sequence selected above, and having avermectin aglycon synthase domain activity.

The above "polypeptide comprising an amino acid sequence wherein one or more amino acids are deleted, replaced or added in the amino acid sequence selected above, and having avermectin aglycon synthase domain activity" can be obtained according to the method described in the above (32) .

(34) A recombinant vector comprising the DNA according to any one of the above (1) to (30) .

(35) A transformant which is obtained by introducing the DNA according to any one of the above (1) to (30) or the recombinant vector of the above (34) into a host cell.

(36) The transformant according to the above (35) wherein the host cell is an avermectin-producing bacterial strain.

(37) The transformant according to the above (35) or (36) wherein the host cell is *Streptomyces avermitilis* K2038 (FERM BP-2775).

(38) A process for producing avermectin aglycon synthase or an avermectin aglycon synthase domain polypeptide comprising:

culturing the transformant according to any one of the above (35) to (37) in a medium to form and accumulate the enzyme or the domain polypeptide in the culture, and

recovering the enzyme or the domain polypeptide from the culture.

(39) A process for producing avermectin aglycon or an altered avermectin aglycon comprising:
culturing the transformant according to any one of the above (35) to (37) in a medium to form and accumulate the avermectin aglycon or the altered avermectin aglycon in the culture, and
recovering the avermectin aglycon or the altered avermectin aglycon from the culture.

(40) A process for producing avermectin or altered avermectin comprising:
culturing the transformant according to any one of the above (35) to (37) in a medium to form and accumulate avermectin aglycon or altered avermectin aglycon in the culture,
glycosylating the avermectin aglycon or altered avermectin glycon, and
recovering avermectin or altered avermectin.

(41) The method according to the above (40) wherein altered avermectin is an avermectin which has been altered from avermectin B1a to avermectin B2a.

(42) An altered avermectin obtainable by the process according to the above (40).

(43) An oligonucleotide having a sequence corresponding to 5 to 60 continuous nucleotides in the nucleotide sequence of the DNA according to the above (1) or (2); or an oligonucleotide having a sequence complementary to the oligonucleotide.

Brief Description of the Drawings

Figure 1 is a restriction enzyme map showing *Bam*HI, *Bgl*II, *Cla*I, *Eco*RI, *Kpn*I, *Mlu*I, *Pst*I, *Stu*I and *Xho*I sites of avermectin aglycon synthase genes, aveAI and aveAII, of *Streptomyces avermitilis*. Each arrow indicates the predicted transcriptional direction of each gene.

Figure 2 shows (1) the chromosomal positions of avermectin aglycon synthase genes and the domain sequences of synthase units, (2) the estimated steps of synthesizing avermectin aglycon, and (3) the structure of 6,8a-seco-6,8a-deoxy-5-oxoAvermectin aglycon synthesized with polyketide synthases, which are the gene products of avermectin aglycon synthase genes aveAI and aveAII, and the positions of lower fatty acids which are incorporated into the skeleton of the compound. In this figure, SU indicates synthase unit, ACP indicates acyl carrier protein, AT indicates an acyltransferase, DH indicates dehydratase, DH* indicates a dehydratase-like domain which is estimated to be inactive, KR indicates β -ketoacyl-ACP reductase, KR* indicates a β –ketoacyl-ACP reductase-like domain which is estimated to be active but is not reflected in the polyketide synthetic reaction, KS indicates β -ketoacyl-ACP synthase, and TE indicates thioesterase.

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Detailed Description of the Invention

The present invention will be described in detail below.

The present invention relates to DNA sequences of genes encoding avermectin aglycon synthase, and a process for producing avermectin aglycon, a basic constitutional unit of avermectin. According to the present invention, it becomes possible to produce a novel avermectin-associated compound or a specific component of avermectins by modification of the DNA to make a change to the type and number of carboxylic acids to be taken in, modification reaction after condensation, or any combination thereof.

1. Preparation of the DNA of the present invention

A DNA encoding avermectin aglycon synthase (an avermectin aglycon synthase gene) can be isolated from bacteria belonging to the genus *Streptomyces*, e.g. *Streptomyces avermitilis*.

Examples of a method for isolating an avermectin aglycon synthase gene include the method described in Japanese Published Unexamined Patent Application No. 15391/91, colony hybridization described in *Molecular Cloning*, Second Edition, etc.

Specific examples include a method which comprises: ligating the partially digested chromosomal DNA of *Streptomyces avermitilis* with appropriate restriction enzyme such as *Sau*3AI, to a cosmid vector capable of replicating in *E.coli* cleaved at a unique restriction enzyme site, e.g. the vector digested with *Bam*HI; transforming *E.coli* with the obtained recombinant DNA; and selecting a transformant having the avermectin aglycon synthase gene from the obtained transformant by colony hybridization.

Examples of DNAs obtained by the above method include DNAs having the nucleotide sequences shown in SEQ ID NOS: 1 and 2.

The DNA having the nucleotide sequence of SEQ ID NO: 1 or 2 was found by chance to be a DNA fragment encoding a portion of polyketide synthase, when a gene encoding avermectin B5-O-methyl transferase (aveD) was isolated (*Gene*, 206, 175-180 (1998)), and was obtained by the above method.

Modules, domains and ORFs, which are relevant to the avermectin aglycon synthase genes of the present invention, can be determined by comparing similarity with the sequences of 3 types of polyketide synthase domains of erythromycin (*Nature*, 348, 176-178 (1990), *Science*, 252, 675-679 (1991), or *Eur. J. Biochem.*, 204, 39-49 (1992)).

Figure 1 shows a restriction map of the avermectin aglycon synthase gene regions (aveAI and aveAII) of genomic DNA (~65kbp) of *Streptomyces avermitilis* together with predicted transcription units (arrow).

Polyketide compounds are natural organic compounds having a variety of structures and functions, and the common characteristics of these compounds are that their synthesis is carried out with a multifunctional enzyme called polyketide synthase.

One polyketide synthase has substrate specificity, and catalyzes the extention of a lower fatty acid constitutional unit (which is used in the form of CoA ester of dicarboxylic acid in reactions other than intial reaction), i.e., condensation to make a polyketide carbon chain, and has a catalytic activity and a controlling activity which modify a β -carbonyl group generated from such a reaction.

The condensation reaction, which is a basic reaction in the synthesis of polyketide, needs various catalytic activities including an acyl carrier protein (ACP) activity, a β -ketoacyl-ACP synthase (KS) activity and an acyltransferase (AT) activity.

In many cases, β -carbonyl groups generated by the condensation reaction are modified. However, depending on a module, some β -carbonyl groups may not be modified and may be used for the next condensation reaction.

Catalytic activities associated with the modification of a β -carbonyl group after the condensation reaction include a β -ketoacyl-ACP reductase (KR) activity, a dehydratase (DH) activity and an enoyl reductase (ER) activity. The biosynthesis of a polyketide chain is terminated by cleaving out the polyketide chain from polyketide synthase by action of thioesterase (TE) activity.

All or several of these modification activities act in each condensation process, thereby determining the structure of a final product.

The avermectin aglycon synthase genes (aveAI and aveAII) of *Streptomyces avermitilis* are characterized in that the genes have several open reading frames each of

which comprises one or more repeating units called a module, just as with other known polyketide biosynthetic genes. A module is defined as a gene fragment which encodes activities for a one-time synthesis, i.e., a one-time condensation reaction, and the subsequent various modification reactions of the β - carbonyl group. Each module encodes ACP, KS and AT associated with the condensation reaction in polyketide synthesis, and all or several of KR, DH and ER associated with the modification reaction of the β - carbonyl group. Furthermore, there is also a module which does not have any domain for a modification reaction. A polypeptide encoding such a module is referred to as synthase unit (SU).

Figure 2 shows a biosynthetic pathway of 6,8a-seco-6,8a-deoxy-5-oxo-avermectin aglycon synthesized with avermectin aglycon synthases of *Streptomyces avermitilis*.

It is clear that PKS-1 is associated with initiation reaction, since an initiation module (SUs), differing from other modules, has acyltransferase (AT) activity on the N-terminal side. It is clear that PKS-3 is associated with the final reaction of polyketide, since module 9 (SU9) has a thioesterase (TE) domain.

The determined DNA sequences comprising avermectin aglycon synthase genes derived from *Streptomyces avermitilis* are shown in SEQ ID NOS: 1 and 2. The DNA of the present invention comprises open reading frames (ORFs) encoding respective multifunctional enzymes, and these ORFs are ORFs corresponding to nucleotide Nos. 11 to 11916 and nucleotide Nos. 211971 to 30688 of SEQ ID NO: 1 and nucleotide Nos. 31 to 14643 and nucleotide Nos. 414824 to 31419 of SEQ ID NO: 2. The amino acid sequences of various peptides encoded by these sequences are shown in SEQ ID NOS: 3, 4, 5 and 6.

Each of the above DNAs comprises a module encoding a synthesis unit

having all catalytic activities necessary for a one-time carbon chain extension reaction. These modules are represented as the following nucleotides in SEQ ID NOS: 1 and 2. That is to say, the modules are represented in SEQ ID NO: 1 as,

Initiation Module: 85 to 1353,

Module 1: 1441 to 6180,

Module 2: 6256 to 11658,

Module 3: 12076 to 15147,

Module 4: 15217 to 19938,

Module 5: 20008 to 24690,

Module 6: 24781 to 30309, and,

are represented in SEQ ID NO: 2 as,

Module 7: 100 to 4692,

Module 8: 4771 to 7818,

Module 9: 7906 to 14619,

Module 10: 14935 to 20334,

Module 11: 20413 to 25734,

Module 12: 25810 to 31125.

The amino acid sequences of various synthase units (SU) encoded by these modules are represented as the following amino acids. That is to say, the sequences are represented in SEQ ID NO: 3 as,

Initiation SU: 29 to 451,

SU1: 481 to 2060,

SU2: 2086 to 3886;

in SEQ ID NO: 4 as,

SU3: 36 to 1059,

SU4: 1083 to 2656,

SU5: 2680 to 4240,

SU6: 4271 to 6113;

in SEQ ID NO: 5 as,
SU7: 34 to 1564,
SU8: 1591 to 2606,
SU9: 2636 to 4873; and,

in SEQ ID NO: 6 as,
SU10: 38 to 1837,
SU11: 1864 to 3637,
SU12: 3663 to 5434.

DNAs encoding Avermectin aglycon synthase domains (submodules) are represented as the following nucleotides. That is to say, the DNAs are represented in SEQ ID NO: 1 as,
in Initiation Module,
ATs: 85 to 1032,
ACPs: 1096 to 1353;

in Module 1,
KS1: 1441 to 2742,
AT1: 3148 to 4068,
KR1: 5143 to 5676,
ACP1: 5935 to 6180;

in Module 2,
KS2: 6256 to 7545,
AT2: 7906 to 8829,
DH2: 8947 to 9384,

KR2: 10609 to 11142,

ACP2: 11413 to 11658;

in Module 3,

KS3: 12076 to 13368,

AT3: 13756 to 14694,

ACP3: 14902 to 15147;

in Module 4,

KS4: 15217 to 16506,

AT4: 16917 to 17862,

KR4: 18886 to 19419,

ACP4: 19693 to 19938;

in Module 5,

KS5: 20008 to 21297,

AT5: 21658 to 22584,

KR5: 23602 to 24138,

ACP5: 24445 to 24690;

in Module 6,

KS6: 24781 to 26079,

AT6: 26413 to 27336,

DH6: 27475 to 27894,

KR6: 29227 to 29760,

ACP6: 30064 to 30309; and,

are also represented in SEQ ID NO: 2 as,

in Module 7,

KS7: 100 to 1383,

AT7: 1648 to 2673,

KR7: 3634 to 4188,

ACP7: 4447 to 4692;

in Module 8,

KS8: 4771 to 6060,

AT8: 6322 to 7344,

ACP8: 7573 to 7818;

in Module 9,

KS9: 7906 to 9258,

AT9: 9676 to 10773,

DH9: 10885 to 11289,

KR9: 12547 to 13104,

ACP9: 13378 to 13659,

TE9: 13879 to 14619;

in Module 10,

KS10: 14935 to 16224,

AT10: 16543 to 17565,

DH10: 17689 to 18066,

KR10: 19285 to 19842,

ACP10: 20089 to 20334;

in Module 11,

KS11: 20413 to 21705,

AT11: 21991 to 23019,

DH11: 23149 to 23529,

KR11: 24685 to 25242,

ACP11: 25489 to 25734;

in Module 12,

KS12: 25810 to 27102,

AT12: 27367 to 28392,

DH12: 28516 to 28878,

KR12: 30076 to 30633,

ACP12: 30880 to 31125.

The deduced amino acid sequences of various domains encoded by these submodules are represented as:

in SEQ ID NO: 3,

ATs: 29 to 344,

ACPs: 366 to 451,

KS1: 481 to 914,

AT1: 1050 to 1356,

KR1: 1715 to 1892,

ACP1: 1979 to 2060,

KS2: 2086 to 2515,

DH2: 2983 to 3128,

KR2: 3537 to 3714,

ACP2: 3805 to 3886;

in SEQ ID NO: 4,

KS3: 36 to 466,

AT3: 596 to 908,

ACP3: 978 to 1059,

KS4: 1083 to 1512,

AT4: 1653 to 1964,

KR4: 2306 to 2483,

ACP4: 2575 to 2656,

KS5: 2680 to 3109,

AT5: 32030 to 3538,

KR5: 3878 to 4056,

ACP5: 4159 to 4240,

KS6: 4271 to 4703,

AT6: 4815 to 5122,

DH6: 5753 to 5930,

ACP6: 6032 to 6113;

in SEQ ID NO: 5,

KS7: 34 to 461,

AT7: 550 to 891,

KR7: 1212 to 1396,

ACP7: 1483 to 1564,

KS8: 1591 to 2020,

AT8: 2108 to 2448,

ACP8: 2525 to 2606,

KS9: 2636 to 3086,

AT9: 3226 to 3591,

DH9: 3629 to 3763,

KR9: 4183 to 4363,

ACP9: 4460 to 4553,

TE9: 4627 to 4873; and,

in SEQ ID NO: 6,

KS10: 38 to 467,

AT10: 574 to 914,

DH10: 956 to 1081,

KR10: 1488 to 1673,

ACP10: 1756 to 1837,

KS11: 1864 to 2294,

AT11: 2390 to 2732,

DH11: 2776 to 2902,

KR11: 3288 to 3473,

ACP11: 3556 to 3637,

KS12: 3663 to 4093,

AT12: 4182 to 4523,

DH12: 4565 to 4685,

KR12: 5085 to 5270,

ACP12: 5353 to 5434.

From a comparison of sequence information regarding the known polyketide synthase genes, it was found that a similarity of sequences exists between domains having identical functions. By using such similarity, it becomes possible to predict the domain of a novel polyketide synthase gene.

In other words, based on the above module, domain and ORF information obtained from DNAs having nucleotide sequences of SEQ ID NO: 1 and 2 derived from *Streptomyces avermitilis*, modules, domains and ORFs, which are relevant to the Avermectin aglycon synthase genes of the present invention derived from other bacteria capable of producing avermectin, can be determined.

Using a DNA having the nucleotide sequence of SEQ ID NO: 1 or 2, an avermectin aglycon synthase gene can be obtained by the following method.

A DNA having the nucleotide sequence of SEQ ID NO: 1 or 2 is digested with appropriate restriction enzymes, the DNA fragment was separated and recovered by the method described in *Molecular Cloning*, Second Edition, and an oligonucleotide consisting of the DNA fragment is used as a probe or primer.

As a probe, the DNA fragment labeled with digoxigenin etc. is preferably used. The DIG labeling & detection kit, which can be purchased from Roche Diagnostic Corp., can be used for labeling with digoxigenin.

A library is prepared from bacteria producing avermectin by genome cloning or cDNA cloning described in *Molecular Cloning*, Second Edition etc.

A clone (or a colony) which is to be cross-hybridized with the probe obtained above is selected from the library, then a plasmid is extracted from the clone by the method described in *Molecular Cloning*, Second Edition, and finally an avermectin aglycon synthase gene can be obtained from the plasmid. In addition, DNAs (i.e. submodules) and modules which encode an avermectin aglycon synthase gene domain can be obtained by the same method.

Otherwise, an avermectin aglycon synthase gene, a submodule and a module can also be obtained by direct PCR amplification, using the above library and primers prepared as above.

In a case where the only partial DNA fragment encoding an avermectin aglycon synthase exists in the plasmid extracted as above, according to standard techniques, a restriction map of the plasmid is prepared by digesting the extracted plasmid with appropriate restriction enzymes such as *Bam*HI.

A restriction enzyme map of a DNA comprising the DNA encoding the entire

avermectin polyketide synthase can be prepared by finding restriction enzyme fragments which commonly exist in several clones and binding up the cloned fragments at overlapping portions, so that the DNA encoding avermectin polyketide synthase can be obtained.

The nucleotide sequence of a DNA encoding avermectin polyketide synthase can be determined by commonly applied nucleotide sequencing analysis, e.g. the dideoxy method (*Proc. Natl. Acad. Sci.* USA, 74, 5463 (1977)), or by the analysis with a DNA sequencing analyzer such as 373A DNA sequencer (Perkin Elmer Corp.).

Specifically, a DNA sequence can be determined by directly using double-stranded plasmid DNA as a template for a cycle sequence reaction, wherein oligonucleotide primers specific for various sequences are used. Alternatively, a DNA sequence can also be determined by: cleaving a DNA fragment into its small fragments; introducing the resulting fragments into bacteria phage M13 at random; preparing an overlapping library, which comprises DNA fragments deleted successively from the termini thereof, using a library or plasmid vector comprising partially overlapping fragments; and subjecting each recombinant DNA fragment to the DNA sequencing using oligonucleotide primers specific to the vector sequence. The fluorescently labeled reactant obtained by the cycle sequence reaction can be analyzed with a DNA sequencer (e.g. Model 4000L, LiCor).

Moreover, based on the nucleotide sequence of the determined DNA, a desired DNA can also be prepared by the chemical synthesis, using a DNA synthesizer (Model 8905, Perceptive BioSystems) etc.

The obtained nucleotide sequence data can be arranged, edited and analyzed using existing software, for example, Genetyx™ (Software Development).

Using the DNAs and DNA fragments of the present invention obtained by the above method, oligonucleotides such as an antisense oligonucleotide and a sense oligonucleotide, which have a portion of the DNA sequence of the present invention, or oligonucleotides comprising an RNA can be prepared according to standard techniques. Alternatively, based on the DNA sequence information obtained as above, these oligonucleotides can also be synthesized with the above-mentioned DNA synthesizer.

Examples of the thus obtained oligonucleotides include a DNA having a sequence corresponding to 5 to 60 continuous nucleotides in the nucleotide sequence of the DNA obtained by the above-mentioned method, or a DNA having a sequence complementary to this DNA. Furthermore, the oligonucleotides of the present invention also include an RNA having a sequence complementary to these DNAs.

Examples of the thus obtained oligonucleotides include a DNA having a sequence corresponding to 5 to 60 continuous nucleotides in the nucleotide sequence of SEQ ID NO: 1 or 2, or a DNA having a sequence complementary to this DNA. Where the oligonucletides are used as sense and antisense primers, from among the above oligonucleotides, it is preferable to apply oligonucleotides wherein melting temperature (Tm) and the number of bases do not significantly differ between both oligonucleotides.

Examples of the thus obtained oligonucleotides include ones having the nucleotide sequences shown in SEQ ID NOS: 9 to 14.

Moreover, the derivatives of these oligonucleotides (hereinafter, also referred to as oligonucleotide derivatives) can also be used as the oligonucleotides of the present invention.

Examples of the oligonucleotide derivatives include: an oligonucleotide derivative obtained by conversion of a phosphodiester phosphate bond into a

phosphorothioate bond in the above-described oligonucleotide; an oligonucleotide derivative obtained by conversion of a phosphodiester bond into a N3'-P5' phosphoamidate bond in the above-described oligonucleotide; an oligonucleotide derivative obtained by conversion of a ribose and a phosphodiester phosphate bond into a peptide nucleic acid bond in the above-described oligonucleotide; an oligonucleotide derivative obtained by substitution of uracil by C-5 propynyl uracil in the above-described oligonucleotide; an oligonucleotide derivative obtained by substitution of uracil by C-5 thiazole uracil in the above-described oligonucleotide; an oligonucleotide derivative obtained by substitution of cytosine by C-5 propynyl cytosine in the above-described oligonucleotide; an oligonucleotide derivative obtained by substitution of cytosine by phenoxazine–modified cytosine in the above-described oligonucleotide; an oligonucleotide derivative obtained by substitution of ribose by 2'-O-propyl ribose in the above-described oligonucleotide; and an oligonucleotide derivative obtained by substitution of ribose by 2'-methoxyethoxy ribose in the above-described oligonucleotide etc. (*Cell Engineering* (*Saibo Kogaku*) 16, 1463 (1997)).

2. Preparation of the polypeptide of the present invention

The polypeptide of the present invention can be produced by using a method described in Molecular Cloning, Second Edition or Current Protocols in Molecular Biology. For example, it can be produced by expressing the DNA of the present invention obtained as described in the above Section 1 in a host cell, according to the following procedure.

Based on the DNA of the present invention, a DNA fragment of an appropriate length containing a region encoding the polypeptide of the present invention can be prepared, if necessary. Further, DNA useful for improving the production efficiency of the polypeptide can be prepared by replacing a nucleotide in the nucleotide sequence of the region encoding the polypeptide so as to make a codon most suitable for expression

in a host cell.

The DNA fragment is inserted at a site downstream of a promoter in an appropriate expression vector to construct a recombinant vector.

The recombinant vector is introduced into a host cell suitable for the expression vector, whereby a transformant producing the polypeptide of the present invention can be obtained.

As a host cell, any bacterial cells, yeast cells, animal cells, insect cells, plant cells etc, that are capable of expressing the desired gene can be used.

As an expression vector, it is possible to use any vector that can autonomously replicate in the above host cells or can be integrated into chromosomes thereof and that contains a promoter at a position appropriate for the transcription of the DNA of the present invention.

When a prokaryote (e.g., a bacterial cell) is used as a host cell, a preferred expression vector for the polypeptide of the present invention may be a recombinant DNA construct that is autonomously replicative in prokaryotes and that comprises a promoter, a ribosome-binding sequence, the DNA of the present invention and a terminator. The vector may further comprise a gene regulating the promoter.

Examples of expression vectors include pBTrp2, pBTac1, pBTac2 (each of which is manufactured by Boehringer Mannheim), pKK233-2 (manufactured by Pharmacia), pGEX (manufactured by Pharmacia), pSE280 (manufactured by Invitrogen), pGEMEX-1 (manufactured by Promega), pQE-8 (manufactured by QIAGEN), pQE-9 (manufactured by QIAGEN), pQE-70 (manufactured by QIAGEN), pQE-60 (manufactured by QIAGEN), pET-3 (manufactured by Novagen), pET-11a

(manufactured by Novagen), pKYP10 (Japanese Published Unexamined Patent Application No. 110600/83), pKYP200 [Agric. Biol. Chem., 48, 669 (1984)], pLSA1 [Agric. Biol. Chem., 53, 277 (1989)], pGEL1 [Proc. Natl. Acad. Sci., USA, 82, 4306 (1985)], pBluescript II SK+ (manufactured by Stratagene), pBluescript II SK(-) (manufactured by Stratagene), pTrS30 [prepared from *E. coli* JM109/pTrS30 (FERM BP-5407)], pTrS32 [prepared from *E. coli* JM109/pTrS32 (FERM BP-5408)], pUC19 [Gene, 33, 103 (1985)], pSTV28 (manufactured by Takara Shuzo Co., Ltd.), pUC118 (manufactured by Takara Shuzo Co., Ltd.), pPA1 (Japanese Published Unexamined Patent Application No. 233798/88), pKC30 (Rosenberg et al., 1983, in "Methods in Enzymology," Vol. 101, pp. 123-138, Academic Press, San Diego), pKK223-3 (manufactured by Pharmacia), pDR540 (manufactured by Pharmacia), pRIT2T (manufactured by Pharmacia), and ptrc99a [Gene, 69, 301 (1988)].

As a promoter, any promoter capable of expressing in host cells, such as *E. coli*, can be used, including promoters derived from *E. coli* or a phage such as *trp* promoter (P*trp*), *lac* promoter (P*lac*), P_L promoter, P_R promoter and P_{SE} promoter, SPO1 promoter, SPO2 promoter, and penP promoter. An artificially designed, modified promoter may also be used, including a promoter obtained by binding two P*trp* promoters in tandem (P*trp* × 2), *tac* promoter, lac T7 promoter, and let I promoter.

It is preferable to use a plasmid having an appropriate distance (e.g., 6-18 bases) between Shine-Dalgarno sequence (i.e., ribosome-binding sequence) and an initiation codon.

A terminator is not necessarily required for expression of the recombinant DNA construct of the present invention, but it is desirably located immediately downstream of a structural gene.

A prokaryote includes a microorganism belonging to *Escherichia*, *Serratia*,

Bacillus, *Brevibacterium*, *Corynebacterium*, *Microbacterium*, *Pseudomonas*, and the like. Specific examples include *Escherichia coli* XL1-Blue, *Escherichia coli* XL2-Blue, *Escherichia coli* DH1, *Escherichia coli* MC1000, *Escherichia coli* KY3276, *Escherichia coli* W1485, *Escherichia coli* JM109, *Escherichia coli* HB101, *Escherichia coli* No.49, *Escherichia coli* W3110, *Escherichia coli* NY49, *Serratia ficaria*, *Serratia fonticola*, *Serratia liquefaciens*, *Serratia marcescens*, *Bacillus subtilis*, *Bacillus amyloliquefaciens*, *Brevibacterium ammoniagenes*, *Brevibacterium immariophilum* ATCC14068, *Brevibacterium saccharolyticum* ATCC14066, *Corynebacterium glutamicum* ATCC13032, *Corynebacterium glutamicum* ATCC14067, *Corynebacterium glutamicum* ATCC13869, *Corynebacterium acetoacidophilum* ATCC13870, *Microbacterium ammoniaphilum* ATCC15354, and *Pseudomonas* sp. D-0110.

Introduction of the recombinant DNA can be carried out by any method for introducing DNA into these host cells: for example, the calcium ion method [Proc. Natl. Acad. Sci. USA, 69, 2110 (1972)], the protoplast method (Japanese Published Unexamined Patent Application No. 248394/88) and electroporation [Nucleic Acids Research., 16, 6127 (1988)].

When a yeast cell is used as a host cell, an expression vector which can be used includes YEp13 (ATCC37115), YEp24 (ATCC37051), YCp50 (ATCC37419), pHS19, pHS15, pG-1, pXT1 (manufactured by Stratagene), pSG5 (manufactured by Stragtagene), pSVK3 (manufactured by Pharmacia), pBPV, pMSG (manufactured by Pharmacia), and pSVL SV40 (manufactured by Pharmacia).

As a promoter, any promoter capable of expressing in yeast cells may be used, including PHO5 promoter, PGK promoter, GAP promoter, ADH promoter, GPD promoter, AOX1 promoter, gal 1 promoter, gal 10 promoter, heat shock polypeptide promoter, MF α 1 promoter, and CUP 1 promoter.

Examples of the host cell include yeast strains belonging to the genus *Saccharomyces*, *Schizosaccharomyces*, *Kluyveromyces*, *Trichosporon*, *Schwanniomyces*, *Pichia* and the like. Specific examples include *Saccharomyces cerevisiae*, *Schizosaccharomyces pombe*, *Kluyveromyces lactis*, *Trichosporon pullulans*, *Schwanniomyces alluvius*, or *Pichia pastoris*.

Introduction of the recombinant DNA can be carried out by any method for introducing DNA into yeast cells: for example, electroporation [Methods in Enzymol., 194, 182 (1990)], the spheroplast method [Proc. Natl. Acad. Sci. USA, 81, 4889 (1984)], the lithium acetate method [J. Bacteriol., 153, 163 (1983)] and the method described in Proc. Natl. Acad. Sci. USA, 75, 1929 (1978).

When an animal cell is used as a host cell, an expression vector which can be used includes pcDNAI, pcDM8 (commercially available from Funakoshi), pAGE107 (Japanese Published Unexamined Patent Application No. 22979/91), pAS3-3 (Japanese Published Unexamined Patent Application No. 227075/90), pCDM8 [Nature, 329, 840 (1987)], pcDNAI/Amp (manufactured by Invitrogen), pREP4 (manufactured by Invitrogen), pAGE103 [J. Biochem, 101, 1307 (1987)], pAGE210, pAMo, and pAMoA.

As a promoter, any promoter capable of expressing in animal cells can be used, including a promoter for immediate early (IE) gene of Cytomegalovirus (CMV), SV40 early promoter or metallothionein promoter, retroviral promoter, heat shock promoter, and SRα promoter. An enhancer for IE gene of Human CMV may also be used together with such a promoter.

Host cells include mouse myeloma cells, rat myeloma cells, mouse hybridoma cells, human Namalwa or Namalwa KJM-1 cells, human fetal kidney cells, human leukemia cells, African green monkey kidney cells, chinese hamster CHO cells, or HBT5637 (Japanese Published Unexamined Patent Application No. 299/88).

Specific examples include SP2/O, NSO and the like for mouse myeloma cells, YB2/O and the like for rat myeloma cells, HEK293 (ATCC: CRL-1573), 293 and the like for human fetal kidney cells, BALL-1 and the like for human leukemia cells, and COS-1, COS-7 and the like for African green monkey kidney cells.

Introduction of the recombinant DNA can be carried out by any method for introducing DNA into animal cells: for example, electroporation [Cytotechnology, 3, 133 (1990)], the calcium phosphate method (Japanese Published Unexamined Patent Application No. 227075/90), the lipofection method [Proc. Natl. Acad. Sci. USA, 84, 7413 (1987)] and the method described in Virology, 52, 456 (1973).

When an insect cell is used as a host cell, a polypeptide can be expressed by a method described in Baculovirus Expression Vectors, A Laboratory Manual, W. H. Freeman and Company, New York (1992); Current Protocols in Molecular Biology; Molecular Biology, A Laboratory Manual; or Bio/Technology, 6, 47 (1988).

More specifically, a recombinant gene transfer vector and a baculovirus may be co-introduced into insect cells to obtain a recombinant virus in the supernatant from the cultured insect cells. Thereafter, insect cells may further be infected with the resulting recombinant virus to express the polypeptide.

Examples of the gene transfer vector used in the above procedure includes pVL1392, pVL1393, pBlueBacIII (commercially available from Invitrogen, respectively) and the like.

Examples of the baculovirus include Autographa californica nuclear polyhedrosis virus, which infects *Noctuidae* insects, and the like.

Examples of insect cells include *Spodoptera frugiperda* ovarian cells, *Trichoplusia ni* ovarian cells, cultured cells derived from silk worm ovary, and the like.

Specific examples are Sf9 and Sf21 (Baculovirus Expression Vectors, A Laboratory Manual) for *Spodoptera frugiperda* ovarian cells, High 5 and BTI-TN-5B1-4 (manufactured by Invitrogen) for *Trichoplusia ni* ovarian cells, *Bombyx mori* N4 for cultured cells derived from silk worm ovary, and the like.

Co-introduction of the recombinant gene transfer vector and the baculovirus into insect cells for recombinant virus production can be carried out by the calcium phosphate method (Japanese Published Unexamined Patent Application No. 227075/90) or the lipofection method [Proc. Natl. Acad. Sci. USA, 84, 7413 (1987)].

When a plant cell is used as a host cell, examples of an expression vector include Ti plasmid, tobacco mosaic virus vector, and the like.

As a promoter, any promoter capable of expressing in plant cells can be used, including cauliflower mosaic virus (CaMV) 35S promoter, rice actin 1 promoter, and the like.

Host cells include plant cells such as tobacco, potato, tomato, carrot, soy bean, Brassica, alfalfa, rice, wheat, barley, and the like.

Introduction of the recombinant vector can be carried out by any method for introducing DNA into plant cells: for example, the *Agrobacterium* method (Japanese Published Unexamined Patent Application No. 140885/84, Japanese Published Unexamined Patent Application No. 70080/85, WO94/00977), electroporation (Japanese Published Unexamined Patent Application No. 251887/85), and the particle gun method (Japanese Patent No. 2606856, Japanese Patent No. 2517813).

The gene can be either expressed directly, or expressed as a secreted polypeptide or a fusion polypeptide according to the method as described in Molecular Cloning, Second Edition. Expression in yeast, animal, insect or plant cells can provide a polypeptide with sugar or sugar chain attached thereto.

The polypeptide of the present invention can be produced by culturing the thus obtained transformant in a medium to produce and accumulate the polypeptide of the present invention in the culture, and recovering the polypeptide from the culture.

The transformant of the present invention can be cultured in a medium according to a conventional method used for culturing host cells.

A medium for culturing a transformant derived from a prokaryote host (e.g., *E. coli*) or a eukaryote host (e.g., yeast) may be a natural or synthetic medium insofar as the medium contains a carbon source, a nitrogen source, an inorganic salt etc., which can be assimilated by the organism, and enables the efficient culture of the transformant.

Any carbon source assimilated by the organisms can be used as a carbon source. Illustrative examples include carbohydrates such as glucose, fructose, sucrose, molasses containing them, starch or starch hydrolysate; organic acids such as acetic acid, propionic acid; alcohols such as ethanol, propanol, and the like.

Examples of the nitrogen source which can be used include ammonium salts of various inorganic or organic acids, such as ammonia, ammonium chloride, ammonium sulfate, ammonium acetate, and ammonium phosphate; other nitrogen-containing compounds; and peptone, meat extracts, yeast extracts, corn steep liquor, casein hydrolysate, soy bean meal, soy bean meal hydrolysate, various fermented cells and hydrolysates thereof and the like.

Inorganic salts which can be used include potassium dihydrogen phosphate, dipotassium hydrogen phosphate, magnesium phosphate, magnesium sulfate, sodium chloride, ferrous sulfate, manganese sulfate, copper sulfate, calcium carbonate, and the like.

Culture is carried out under aerobic conditions by shaking culture, submerged spinner culture under aeration, and the like. The culture temperature is preferably from 15 to 40°C, and culturing time is usually from 5 hours to 7 days. During the culture, pH is maintained at 3.0 to 9.0. The pH can be adjusted using an inorganic or organic acid, an alkaline solution, urea, calcium carbonate, ammonia and the like.

Also, if necessary, antibiotics such as ampicillin and tetracycline can be added to a medium during the culturing.

In a case where a microorganism is transformed with an expression vector containing an inducible promoter, the transformant can be cultured in a medium supplemented with an inducer, if necessary. For example, when an expression vector containing *lac* promoter is used for transformation, the transformant may be cultured in a medium supplemented with isopropyl-β-D-thiogalactopyranoside or the like; when an expression vector containing *trp* promoter is used for transformation, the transformant can be cultured in a medium supplemented with indole acrylic acid or the like.

A medium for culturing a transformant obtained using an animal cell as the host includes generally-used media such as RPMI 1640 medium [The Journal of the American Medical Association, 199, 519 (1967)], Eagle's MEM medium [Science, 122, 501 (1952)], DMEM medium [Virology, 8, 396 (1959)], 199 medium [Proceeding of the Society for the Biological Medicine, 73, 1 (1950)] as well as other media to which fetal calf serum or the like has been added to the above media and the like.

Culturing is generally carried out at pH 6 to 8, at a temperature of 25 to 40°C for a period of 1 to 7 days in the presence of 5% CO_2.

Also, if necessary, antibiotics such as kanamycin, penicillin and streptomycin may be added to a medium during the culturing.

A medium for culturing a transformant obtained using an insect cell as the host includes generally-used media such as TNM-FH medium (manufactured by PharMingen), Sf-900 II SFM medium (manufactured by Life Technologies), ExCell 400 and ExCell 405 [both being products of JRH Biosciences], Grace's Insect Medium [Nature, 195, 788 (1962)] or the like.

Culturing is generally carried out at pH 6 to 7, at a temperature of 25 to 30°C for a period of 1 to 5 days.

Also, if necessary, antibiotics such as gentamycin can be added to a medium during the culture.

The transformant obtained using a plant cell as the host can be cultured as a cell or can be allowed to differentiate into plant cell or organ before culture. Examples of the medium for culturing the transformant include a generally used medium such as Murashige and Skoog (MS) medium, White medium, or any one of these media further supplemented with a plant hormone such as auxin or cytokinin.

Culturing is carried out usually at pH 5 to 9, at a temperature of 20 to 40°C for a period of 3 to 60 days.

Also, if necessary, antibiotics such as kanamycin and hygromycin can be added

to a medium during the culturing.

As described above, the polypeptide of the present invention can be produced by culturing a microorganism-, animal cell-, or plant cell-derived transformant carrying a recombinant vector in which a DNA encoding the polypeptide of the present invention has been inserted according to a general manner to produce and accumulate the polypeptide, and then recovering the polypeptide from the culture.

A method for producing the polypeptide of the present invention includes intracellular production in host cells, extracellular secretion by host cells or production on outer membranes of host cells, and the method can be selected depending on the type of host cells to be used and/or the structure of polypeptide to be produced.

If the polypeptide of the present invention is produced in host cells or on outer membranes of host cells, the polypeptide can be efficiently secreted to extracellularly from the host cells by using the method of Paulson et al. [J. Biol. Chem., 264, 17619 (1989)], the method of Lowe et al. [Proc. Natl. Acad. Sci., USA, 86, 8227 (1989), Genes Develop., 4, 1288 (1990)] or methods as described in Japanese Published Unexamined Patent Application No. 336963/93 and PCT WO94/23021.

More specifically, the polypeptide of the present invention can be efficiently secreted from host cells by expressing it in a form with signal peptide using genetic recombination techniques, the signal peptide being added upstream of a portion containing the active site of the polypeptide of the present invention.

Furthermore, the amount of the production can be increased using a gene amplification system using a dihydrofolate reductase gene or the like according to the method described in Japanese Published Unexamined Patent Application No. 227075/90.

Further, animal or plant cells introduced with a gene may be re-differentiated to create an animal individual carrying a transgene (transgenic non-human animal) or a plant individual carrying a transgene (transgenic plant), which may be used for producing the polypeptide of the present invention.

When the transformant is an animal or plant individual, the polypeptide may be obtained by feeding or cultivating the individual in a general manner to produce and accumulate the polypeptide, and then recovering the polypeptide from the animal or plant individual.

The methods for producing the polypeptide of the present invention using an animal individual include a method using an animal obtained by introducing a gene in accordance with known manners as described in American Journal of Clinical Nutrition, 63, 639S (1996); American Journal of Clinical Nutrition, 63, 627S (1996); and Bio/Technology, 9, 830 (1991).

In the case of an animal individual, for example, the polypeptide of the present invention may be obtained by feeding a transgenic non-human animal introduced with a DNA insert encoding the polypeptide of the present invention to produce and accumulate therein the polypeptide, and then recovering the polypeptide from the animal. The polypeptide can be produced and accumulated in the animal's milk (Japanese Published Unexamined Patent Application No. 309192/88), egg, and the like. As a promoter used for this purpose, any promoter can be used so long as it can be expressed in the animal, for example, mammary gland cell-specific promoters such as an α-casein promoter, a β-casein promoter, a β-lactoglobulin promoter and a whey acidic protein promoter being preferred.

The methods for producing the polypeptide of the present invention using a

plant individual include a method cultivating a transgenic plant obtained by introducing a gen encoding the polypeptide of the present invention to produce and accumulate therein the polypeptide in a known manner as described in Tissue Culture (Soshiki Baiyo), 20 (1994); Tissue Culture, 21 (1995); and Trends in Biotechnology, 15, 45 (1997), and then the polypeptide can be recovered from the plant.

For isolation and purification of the polypeptide produced by the transformant of the present invention, conventional methods for the isolation and purification of enzymes can be used.

For example, if the polypeptide of the present invention is expressed in a soluble form in cells, after completion of culturing, the cells are recovered by centrifugation, and suspended in an aqueous buffer and then disrupted with ultrasonic disrupter, French Press, Manton-Gaulin homogenizer, Dynomill or the like, to obtain a cell-free extract.

From the supernatant obtained by centrifuging the cell-free extract, a purified product can be obtained by the general method used for isolating and purifying an enzyme, for example, solvent extraction, salting-out using ammonium sulfate or the like, desalting, precipitation using an organic solvent, anion exchange chromatography using a resin, such as diethylaminoethyl (DEAE)-Sepharose, DIAION HPA-75 (manufactured by Mitsubishi Chemical) or the like, cation exchange chromatography using a resin, such as S-Sepharose FF (manufactured by Pharmacia) or the like, hydrophobic chromatography using a resin, such as butyl sepharose, phenyl sepharose or the like, gel filtration using a molecular sieve, affinity chromatography, chromatofocusing, or electrophoresis, such as isoelectronic focusing or the like, alone or in combination thereof.

When the protein is expressed as an inclusion body in the host cells, the cells are collected in the same manner, disrupted and centrifuged to recover the inclusion body of the protein as the precipitate fraction. Next, the inclusion body of the protein is solubilized with a protein-denaturing agent.

The solubilized protein solution is diluted with or dialyzed against a solution containing no protein-denaturing agent or such a dilute solution containing the protein-denaturing agent at a lower concentration that denaturation of the protein is not caused. Thus, the normal tertiary structure of the protein is reconstituted. After the procedure, a purified product of the protein can be obtained by a purification and isolation method similar to the above.

When the protein of the present invention or its glycosylated-derivative is secreted out of cells, the protein or its derivative can be collected from the culture supernatant.

Namely, the culture supernatant is obtained by treating the culture in a similar manner to the above-mentioned centrifugation or the like. Then, a purified product can be obtained from the supernatant using a purification and isolation method similar to the above.

Examples of the thus obtained protein include a protein comprising the amino acid sequence represented by SEQ ID NO:1.

Furthermore, a fusion protein of the protein of the present invention and other protein may be produced, and purified by affinity chromatography using a substance having affinity to the fusion protein. For example, the protein of the present

invention may be produced as a fusion protein with protein A according to the method of Lowe *et al.* (*Proc. Natl. Acad. Sci. USA*, *86*: 8227 (1989); *Genes Develop.*, *4*: 1288 (1990)), or the method described in Japanese Published Unexamined Patent Application No. 336963/93 or 823021/94, and purified by affinity chromatography using immunoglobulin G.

Moreover, the protein of the present invention may be produced as a fusion protein with Flag peptide, and the fusion protein can be purified by affinity chromatography using an anti-Flag antibody (*Proc. Natl. Acad. Sci., USA*, *86*: 8227 (1989), *Genes Develop.*, *4*: 1288 (1990)). Further purification can be carried out by affinity chromatography using the antibody against the protein *per se*.

Also, based on the information of the thus obtained protein, the protein of the present invention can be produced by the chemical synthesis method, such as Fmoc (fluorenylmethyloxycarbonyl) method, tBoc (t-butyloxycarbonyl) method, or the like. It can also be chemically synthesized using a peptide synthesizer manufactured by Advanced ChemTech, Perkin-Elmer, Pharmacia, Protein Technology Instrument, Synthecell-Vega, PerSeptive, Shimadzu Corporation, or the like.

3. Production of Avermectin aglycon or Avermectin

Avermectin aglycon can be produced by culturing the transformant prepared in the above Section 2, which carries the avermectin aglycon synthase gene or a module or submodule thereof, in a medium to produce and accumulate avermectin aglycon in the culture, and then recovering avermectin aglycon from the culture.

When a host used for preparation of a transformant can produce avermectin, avermectin aglycon or avermectin can be efficiently produced in any one of the transformants obtained by introducing the avermectin aglycon synthase gene or a

module or submodule thereof into the host. The transformant thus obtained can produce avermectin aglycon or avermectin with higher efficiency than that of the host.

When a host used for preparation of a transformant cannot produce avermectin, the avermectin aglycon synthase gene may be introduced into the host to obtain a transformant capable of producing avermectin aglycon.

In the production of avermectin or avermectin aglycon, the above transformant can be cultured according to a culture procedure as described in the above Section 2.

A known avermectin is a macrocyclic lactone having a 16-membered ring with two sugar residues attached thereto via glycosidic linkage. Avermectin aglycon can be converted into avermectin in a manner well known in the art, for example, by glycosylating avermectin aglycon as described in J. Bacteriol., 175, 2552-2563 (1993).

4. Production of modified Avermectin aglycon or Avermectin

Avermectin aglycon is formed through extension of lower-fatty acid units (used in the form of CoA ester of dicarboxylic acid in reactions other than the initial reaction) by avermectin aglycon synthase, i.e., condensation to give a polyketide carbon chain, and modification of β-carbonyl groups generated during the condensation.

As described above, the avermectin aglycon synthase gene is composed of modules, each module comprising DNA encoding avermectin aglycon synthase domains (submodule).

A submodule encodes ACP, KS and AT involved in condensation during polyketide synthesis, as well as KR, DH or ER involved in modification of β-carbonyl groups.

Accordingly, the carbon chain length of the aglycon part and the type of functional group on β-carbon in the condensation process can be altered by modifying a submodule, based on nucleotide sequence information of the Avermectin aglycon synthase gene determined in the above Section 1.

Further, selective inactivation of a submodule can result in production of a predictable novel avermectin or a particular component thereof alone.

By way of example, a strain producing avermectin B1a and B2a, *Streptomyces avermitilis* K2038, can be converted into a strain producing only avermectin B2a by replacing or converting a submodule DH2 region of the avermectin aglycon synthase gene by or into its inactivated form without dehydratase activity.

The submodule DH2 region can be replaced by or converted into its inactivated form, for example, by homologous recombination on submodule DH2 of the above strain to give the nucleotide sequence shown in SEQ ID NO: 7 in a general manner as described in Molecular Cloning, Second Edition.

The strain thus obtained, which becomes capable of producing a modified (or altered) avermectin aglycon, can be used to produce and obtain the modified avermectin aglycon or modified avermectin according to the general process for producing avermectin.

Best Modes for Carrying Out the Invention

The following examples are provided for illustrative purposes only, and are not intended to limit the scope of the invention clearly defined above.

Example 1: Determination of the nucleotide sequence of the Avermectin aglycon synthase gene of *Streptomyces avermitilis*

A nucleotide sequence of the DNA encoding avermectin aglycon synthase derived from *Streptomyces avermitilis* K2033 (US Patent No. 5206155, FERM BP-2773) was determined as follows.

Continuous or overlapping DNA fragments within the avermectin aglycon synthase gene were subcloned from plasmids containing a fragment of the avermectin aglycon synthase genes (aveAI and aveAII) co-isolated with a gene encoding avermectin B5-O-transmethylase (aveD; Gene, 206, 175-180 (1998)). Nucleotide sequences of the inserted DNA fragments in these subclones were then determined.

More specifically, the entire nucleotide sequences of aveAI and aveAII were determined by subcloning BamHI-treated fragments of 3.4 kbp, 2.0 kbp, 0.5 kbp, 6.8 kbp, 7.0 kbp, 7.8 kbp, 3.7 kbp, 4.8 kbp, 1.3 kbp, 2.4 kbp, 0.7 kbp, 1.0 kbp, 5.4 kbp, 2.5 kbp, 1.9 kbp, 0.1 kbp, 7.0 kbp, 3.1 kbp, 4.7 kbp and 1.3 kbp found in the BamHI-restriction map of aveAI and aveAII shown in Figure 1; treating the inserted DNA fragments in these subclones with exonuclease III and S1 nuclease to prepare a series of deletion fragments; and then carrying out a cycle-sequencing reaction using fluorescently-labeled primers to determine a nucleotide sequence of each deletion fragment. The genes aveAI and aveAII had the nucleotide sequences shown in SEQ ID NO: 1 and SEQ ID NO: 2, respectively.

Example 2: Production of Avermectin B2a alone by nucleotide modification of dehydratase domain in module 2

Streptomyces avermitilis K2033 (FERM BP-2775) produces avermectin B1a and B2a.

The information of avermectin aglycon synthase genes (SEQ ID NOs: 1 and 2) derived from the avermectin-producing strain, which were obtained and sequenced in Example 1, indicated that avermectin was biosynthesized through the biosynthetic

pathway shown in Figure 2.

Avermectin B1a differs from avermectin B2a only in that avermectin B1a has a double bond between 22- and 23-positions in its aglycon part, while avermectin B2a has a single bond between 22- and 23-positions and a hydroxyl group at 23-position in its aglycon part.

The biosynthetic pathway for avermectin found above indicated that avermectin aglycon synthase domain DH of SU2 (DH2) is responsible for the formation of a double bond between 22- and 23-positions in the aglycon part of avermectin B1a and that avermectin aglycon synthase domain DH of SU10 (DH10) has no dehydratase activity.

Based on the idea that a strain producing only avermectin B2a could be obtained by converting DH2 into a domain without dehydratase activity like DH10, DH2 without dehydratase activity was prepared as follows.

The Avermectin aglycon synthase genes obtained in Example 1 had six DH domains: DH2, DH6, DH9, DH10, DH11 and DH12. Comparisons of nucleotide sequences of these domains showed that DH10 clearly differed from other DH domains in a consensus sequence common to dehydratase.

More specifically, amino acid sequences of DH2, DH6, DH9, DH11 and DH12, which were directly involved in the avermectin aglycon formation, were shown to include a consensus sequence of HXaaXaaXaaGXaaXaaXaaXaaP (SEQ ID NO: 13) or HXaaXaaXaaGXaaXaaXaaXaaS (SEQ ID NO: 14), wherein H, G, P, S and Xaa represent histidine, glycine, proline, serine and any amino acid, respectively; whereas the corresponding sequence of DH10 was YXaaXaaXaaGXaaXaaXaaXaaS (SEQ ID NO: 15), wherein Y represents tyrosine, and Xaa, G and S are as defined above.

Thus, replacement of an N-terminal H (His) by Y (Tyr) was thought to provide dehydratase without its activity.

A DNA was constructed, which had a nucleotide sequence encoding the sequence for replacement of the N-terminal amino acid sequence -His-Ala- in the consensus sequence of DH2 [-His-Ala-Val-Gly-Gly-Thr-Val-Leu-Leu-Ser- (SEQ ID NO: 16), amino acids 3037-3046 in SEQ ID NO: 3] by the corresponding sequence of DH10: -Tyr-Glu- (amino acids 1008-1017 in SEQ ID NO: 6). That is, the DNA sequence of DH2 domain: 5'-CAT GCC-3' (nucleotides 9109-9114 in SEQ ID NO: 1) was replaced by the sequence: 5'-TAC GAG-3' as follows.

A DNA fragment of the aveAI region containing DH2 domain was digested with restriction enzyme *Sma*I, and the 2327 bp *Sma*I fragment corresponding to nucleotides 7869-10196 in SEQ ID NO: 1 was cloned into the *Sma*I site of vector plasmid pUC19.

Taq DNA polymerase buffer, dATP, dGTP, dCTP, dTTp and Taq DNA polymerase were added to the resulting recombinant plasmid, which was then divided into two aliquots.

To one of these two aliquots, a primer having the nucleotide sequence shown in SEQ ID NO: 9 (corresponding to nucleotides 9098-9127 in SEQ ID NO: 1) and an antisense primer having the nucleotide sequence shown in SEQ ID NO: 10 (corresponding to an antisense of nucleotides 9193-9222 in SEQ ID NO: 1) were added.

To the other aliquot, an antisense primer having the nucleotide sequence shown in SEQ ID NO: 11 (corresponding to an antisense of nucleotides 9098-9127 in SEQ ID NO: 1) and a primer having the nucleotide sequence shown in SEQ ID NO: 12

(corresponding to nucleotides 8948-8977 in SEQ ID NO: 1) were added.

After the addition, each aliquot was treated at 96 °C for 5 minutes, and the reaction was repeated for 5 to 10 cycles under the following conditions: at 98 °C for 15 seconds and 68 °C for 30 seconds per cycle.

After the reaction, exonuclease I and alkaline phosphatase were added to each aliquot, incubated at 37 °C for 15 minutes, and then treated at 80 °C for 10 minutes to inactivate both the enzymes.

After the inactivation of both the enzymes, Taq DNA polymerase buffer, dATP, dGTP, dCTP, dTTp, a primer having the nucleotide sequence of SEQ ID NO: 12 (corresponding to nucleotides 8948-8977 in SEQ ID NO: 1), an antisense primer having the nucleotide sequence of SEQ ID NO: 10 (corresponding to an antisense of nucleotides 9193-9222 in SEQ ID NO: 1) and Taq DNA polymerase were added to each reaction solution. Each reaction solution was then treated at 96 °C for 5 minutes, and the reaction was repeated for 25 cycles under the following conditions: at 98 °C for 15 seconds and 68 °C for 30 seconds per cycle.

After the reaction, exonuclease I and alkaline phosphatase were added to each reaction solution, incubated at 37 °C for 15 minutes, and then treated at 80 °C for 10 minutes to inactivate the enzymes.

After the inactivation of the enzymes, restriction enzymes *Xcm*I and *Bsa*AI were added to each reaction solution to obtain a *Xcm*I-*Bsa*AI treated DNA fragment.

Restriction enzymes *Xcm*I and *Bsa*AI were added to the recombinant plasmid prepared above, which carried the inserted 2327 bp *Sma*I fragment, to obtain a *Xcm*I-*Bsa*AI treated vector fragment. The *Xcm*I-*Bsa*AI treated vector fragment, T4

DNA ligase buffer, ATP and T4 DNA ligase were added to the *Xcm*I-*Bsa*AI treated DNA fragment, and then incubated overnight at 22 °C to ligate these fragments together, thereby obtaining a plasmid carrying the inserted *Xcm*I-*Bsa*AI treated DNA fragment.

After the transformation of *E. coli* cells with the plasmid, the recombinant plasmids were extracted from individual colonies, and each DNA fragment inserted into the vector was then confirmed for its nucleotide sequence, thereby selecting a clone carrying a fragment introduced with the intended nucleotide replacement.

The inserted DNA fragment was taken from the selected clone, and then carried out recombination with DH2 region on the chromosome of *Streptomyces avermitilis* K2038 by homologous recombination according to a method as described in Japanese Published Examined Patent Application No. 344605/92.

The resulting recombinant *Streptomyces avermitilis* K2210 was cultured under the conditions for general avermectin production, and then the resulting cells were extracted with methanol.

The resulting extract was analyzed using two procedures presented below.

(1) Procedure using thin-layer chromatography on silica gel

Chromatography condition: silica gel, Merck Silica Gel plate F254 (Merck Corp.)

Development solution: n-hexane/iso-propyl alcohol = 85/15

Detection: UV

(2) Procedure using high performance liquid chromatography

Chromatography condition: column, ODS-Hypersil-3 (Elmer Corp.)

Mobile phase: acetonitrile/methanol/water = 60/14/26

Flow rate: 0.6 ml/min

Detection: 246 nm

Temperature: room temperature

In both analytical procedures, only the same peak as that of avermectin B2a was observed. Further, the culture extract was purified by chromatographies on Sephadex LH-20 and silica gel to give the purified product. The purified product was analyzed by NMR and mass spectrometry, indicating that the above recombinant strain produced only avermectin B2a.

Namely, avermectin B2a alone could be produced and obtained according to the method as described above.

EP 0 954 595 B1

Industrial Applicability

The present invention can provide the DNAs encoding a multifunctional enzyme involved in the biosynthesis of avermectin compound useful as a pharmaceutical agent, a veterinary agent and a agricultural chemical; polypeptides encoded by the DNAs; vectors comprising the DNAs; a host cell transformed with the DNA or vector; and a process for producing avermectin or modified avermectin.

Sequence Listing Free Text

SEQ ID NO: 9 represents a primer based on the sequence between nucleotides 9098 and 9127 in SEQ ID NO: 1

SEQ ID NO: 10 represents an antisense primer based on the sequence between nucleotides 9193 and 9222 in SEQ ID NO: 1

SEQ ID NO: 11 represents an antisense primer based on the sequence between nucleotides 9098 and 9127 in SEQ ID NO: 1

SEQ ID NO: 12 represents a primer based on the sequence between nucleotides 8948 and 8977 in SEQ ID NO: 1

The scope of the present invention will be defined by the appended claims, and

it will be appreciated that other numerous variations and modifications may be made without departing from the spirit or scope of the invention. The above examples are therefore to be construed in all respects as illustrative and not restrictive. Further, equivalents of the claims will also fall within the scope of the present invention.

All of patents, patent applications and other publications cited in this specification and the contents as disclosed in the specification and/or drawings of Japanese Patent Application No. 046961/99, which is a priority document of the present application, are incorporated herein by reference in their entirety.

Docket No. 98-1-0

WHAT IS CLAIMED IS:

1. A DNA encoding avermectin aglycon synthase.

2. A DNA comprising a nucleotide sequence selected from the group consisting of nucleotide Nos. 1-11916 and 11971-30688 of SEQ ID NO: 1 and nucleotide Nos. 1-14643 and 14824-31419 of SEQ ID NO: 2; or
a DNA which hybridizes with said DNA under stringent conditions and which encodes a polypeptide having avermectin aglycon synthase activity.

3. The DNA according to claim 1 or 2 wherein the DNA comprises DNAs encoding avermectin aglycon synthase domains.

4. The DNA according to claim 3 wherein the DNAs encoding avermectin aglycon synthase domains are selected from the group consisting of:
a DNA encoding a polypeptide having acyltransferase activity and acyl carrier protein activity;
a DNA encoding a polypeptide having β-ketoacyl-ACP synthase activity, acyltransferase activity, β-ketoacyl-ACP reductase activity and acyl carrier protein activity;
a DNA encoding a polypeptide having β-ketoacyl-ACP synthase activity, acyltransferase activity, dehydratase activity, β-ketoacyl-ACP reductase activity and acyl carrier protein activity;
a DNA encoding a polypeptide having β-ketoacyl-ACP synthase activity, acyltransferase activity, and acyl carrier protein activity; and
a DNA encoding a polypeptide having β-ketoacyl-ACP synthase activity, acyltransferase activity, dehydratase activity, β-ketoacyl-ACP reductase activity, acyl carrier protein activity, and thioesterase activity.

5. The DNA according to claim 4 wherein the DNA encoding a polypeptide having acyltransferase activity and acyl carrier protein activity is the DNA comprising a nucleotide sequence of nucleotide Nos. 85-1353 of SEQ ID NO: 1; or
a DNA which hybridizes with said DNA under stringent conditions and which encodes a polypeptide having acyltransferase activity and acyl carrier protein activity.

6. The DNA according to claim 4 wherein the DNA encoding a polypeptide having β-ketoacyl-ACP synthase activity, acyltransferase activity, β-ketoacyl-ACP reductase activity, and acyl carrier protein activity is:
a DNA comprising the nucleotide sequence selected from the group consisting of nucleotide Nos. 1441-6180, 15217-19938 and 20008-24690 of SEQ ID NO: 1, and nucleotide Nos. 100-4692 and 14935-20334 of SEQ ID NO: 2; or
a DNA which hybridizes with said DNA under stringent conditions and which encodes a polypeptide having β-ketoacyl-ACP synthase activity, acyltransferase activity, β-ketoacyl-ACP reductase activity, and acyl carrier protein activity.

7. The DNA according to claim 4 wherein the DNA encoding a polypeptide having β-ketoacyl-ACP synthase activity, acyltransferase activity, dehydratase activity, β-ketoacyl-ACP reductase activity, and acyl carrier protein activity is:
a DNA comprising the nucleotide sequence selected from the group consisting of nucleotide Nos. 6256-11658 and 24781-30309 of SEQ ID NO: 1, and nucleotide Nos. 20413-25734 and 25810-31125 of SEQ ID NO: 2; or
a DNA which hybridizes with said DNA under stringent conditions and which encodes a polypeptide having β-ketoacyl-ACP synthase activity, acyltransferase activity, dehydratase activity, β-ketoacyl-ACP reductase activity, and acyl carrier protein activity.

8. The DNA according to claim 4 wherein the DNA encoding a polypeptide having β-ketoacyl-ACP synthase activity, acyltransferase activity, and acyl carrier

protein activity is:

a DNA comprising the nucleotide sequence of nucleotide No. 12076-15147 of SEQ ID NO: 1, or nucleotide No. 4771-7818 of SEQ ID NO: 2;

or a DNA which hybridizes with said DNA under stringent conditions and which encodes a polypeptide having β-ketoacyl-ACP synthase activity, acyltransferase activity, and acyl carrier protein activity.

9. The DNA according to claim 4 wherein the DNA encoding polypeptides having β-ketoacyl-ACP synthase activity, acyltransferase activity, dehydratase activity, β-ketoacyl-ACP reductase activity, acyl carrier protein activity, and thioesterase activity is:

a DNA comprising the nucleotide sequence of nucleotide Nos. 7906-14619 of SEQ ID NO: 2; or

a DNA which hybridizes with said DNA under stringent conditions and which encodes a polypeptide having β-ketoacyl-ACP synthase activity, acyltransferase activity, dehydratase activity, β-ketoacyl-ACP reductase activity, acyl carrier protein activity, and thioesterase activity.

10. The DNA according to claim 4 wherein the DNA encoding a polypeptide having acyltransferase activity is:

a DNA comprising the nucleotide sequence selected from the group consisting of nucleotide Nos. 85-1032, 7906-8829, 13756-14694, 16917-17862, 21658-22584, and 26413-27336 of SEQ ID NO: 1, and nucleotide Nos. 1648-2673, 6322-7344, 9676-10773, 16543-17565, 21991-23019 and 27367-28392 of SEQ ID NO: 2; or

a DNA which hybridizes with said DNA under stringent conditions and which encodes a polypeptide having acyltransferase activity.

11. The DNA according to claim 4 wherein the DNA encoding a polypeptide having acyl carrier protein activity is:

a DNA comprising the nucleotide sequence selected from the group consisting of nucleotide Nos. 1096-1353, 5935-6180, 11413-11658, 14902-15147, 19693-19938, 24445-24690 and 30064-30309 of SEQ ID NO: 1, and nucleotide Nos. 4447-4692, 7573-7818, 13378-13659, 20089-20334, 25489-25734 and 30880-31125 of SEQ ID NO: 2; or

a DNA which hybridizes with said DNA under stringent conditions and which encodes a polypeptide having acyl carrier protein activity.

12. The DNA according to claim 4 wherein the DNA encoding a polypeptide having β-ketoacyl-ACP synthase activity is:

a DNA comprising the nucleotide sequence selected from the group consisting of nucleotide Nos. 1441-2742, 6256-7545, 12076-13368, 15217-16506, 20008-21297 and 24781-26079 of SEQ ID NO: 1, and nucleotide Nos. 100-1383, 4771-6060, 7906-9258, 14935-16224, 20413-21705 and 25810-27102 of SEQ ID NO: 1; or

a DNA which hybridizes with said DNA under stringent conditions and which encodes a polypeptide having β-ketoacyl-ACP synthase activity.

13. The DNA according to claim 4 wherein the DNA encoding a polypeptide having β-ketoacyl-ACP reductase activity is:

a DNA comprising the nucleotide sequence selected from the group consisting of nucleotide Nos. 5143-5676, 10609-11142, 18886-19419, 23602-24138 and 29227-29760 of SEQ ID NO: 1, and nucleotide Nos. 3634-4188, 12547-13104, 19285-19842, 24685-25242 and 30076-30633 of SEQ ID NO: 2; or

a DNA which hybridizes with said DNA under stringent conditions and which encodes a polypeptide having β-ketoacyl-ACP reductase activity.

14. The DNA according to claim 4 wherein the DNA encoding a polypeptide having dehydratase activity is:

a DNA comprising the nucleotide sequence selected from the group consisting of

nucleotide Nos. 8947-9384 and 27475-27894 of SEQ ID NO: 1, and nucleotide Nos. 10885-11289, 23149-23529 and 28516-28878 of SEQ ID NO: 2; or

a DNA which hybridizes with said DNA under stringent conditions and which encodes a polypeptide having dehydratase activity.

15. The DNA according to claim 4 wherein the DNA encoding a polypeptide having thioesterase activity is:

a DNA comprising the nucleotide sequence of nucleotide No. 13879-14619 of SEQ ID NO: 2; or

a DNA which hybridizes with said DNA under stringent conditions and which encodes a polypeptide having thioesterase activity.

16. The DNA according to claim 3 or 4 wherein the DNA encoding avermectin aglycon synthase domains is a mutated DNA encoding a polypeptide having enhanced or diminished activity of the domain.

17. The DNA according to claim 16 wherein the DNA encoding a polypeptide having diminished activity of Avermectin aglycon synthase domain is a DNA comprising the nucleotide sequence of SEQ ID NO: 7.

18. A DNA encoding an Avermectin aglycon synthase domain which comprises a nucleotide sequence selected from the group consisting of: nucleotide Nos. 85-1032, 1096-1353, 1441-2742, 3148-4068, 5143-5676, 5935-6180, 6256-7545, 7906-8829, 8947-9384, 10609-11142, 11413-11658, 12076-13368, 13756-14694, 14902-15147, 15217-16506, 16917-17862, 18886-19419, 19693-19938, 20008-21297, 21658-22584, 23602-24138, 24445-24690, 24781-26079, 26413-27336, 27475-27894, 29227-29760 and 30064-30309 of SEQ ID NO: 1, and nucleotide Nos. 100-1383, 1648-2673, 3634-4188, 4447-4692, 4771-6060, 6322-7344, 7573-7818, 7906-9258, 9676-10773, 10885-11289, 12547-13104, 13378-13659, 13879-14619, 14935-16224, 16543-17565,

17689-18066, 19285-19842, 20089-20334, 20413-21705, 21991-23019, 23149-23529, 24685-25242, 25489-25734, 25810-27102, 27367-28392, 28516-28878, 30076-30633 and 30880-31125 of SEQ ID NO: 2; or

a DNA which hybridizes with said DNA under stringent conditions and which encodes a polypeptide having avermectin aglycon synthase domain activity.

19. A DNA comprising the nucleotide sequence of nucleotide No. 85-1353 of SEQ ID NO: 1 ;or

a DNA which hybridizes with said DNA under stringent conditions and which encodes a polypeptide having acyltransferase activity and acyl carrier protein activity.

20. A DNA comprising the nucleotide sequence selected from the group consisting of nucleotide Nos. 1441-6180, 15217-19938, and 20008-24690 of SEQ ID NO: 1, and nucleotide Nos. 100-4692 of SEQ ID NO: 2; or

a DNA which hybridizes with said DNA under stringent conditions and which encodes a polypeptide having β-ketoacyl-ACP synthase activity, acyltransferase activity, β-ketoacyl-ACP reductase activity and acyl carrier protein activity.

21. A DNA comprising the nucleotide sequence selected from the group consisting of nucleotide Nos. 6256-11658, and 24781-30309 of SEQ ID NO: 1, and nucleotide Nos. 14935-20334, 20413-25734 and 25810-31125 of SEQ ID NO: 2; or

a DNA which hybridizes with said DNA under stringent conditions and which encodes a polypeptide having β-ketoacyl-ACP synthase activity, acyltransferase activity, dehydratase activity, β-ketoacyl-ACP reductase activity and acyl carrier protein activity.

22. A DNA comprising the nucleotide sequence of nucleotide No. 12076-15147 of SEQ ID NO: 1, or the nucleotide sequence of nucleotide No. 4771-7818 of SEQ ID NO: 2; or

a DNA which hybridizes with said DNA under stringent conditions and which encodes

a polypeptide having β-ketoacyl-ACP synthase activity, acyltransferase activity, and acyl carrier protein activity.

23. A DNA comprising the nucleotide sequence of nucleotide No. 7906-14619 of SEQ ID NO: 2; or

a DNA which hybridizes with said DNA under stringent conditions and which encodes a polypeptide having β-ketoacyl-ACP synthase activity, acyltransferase activity, dehydratase activity, β-ketoacyl-ACP reductase activity, acyl carrier protein, and thioesterase activity.

24. A DNA comprising the nucleotide sequence selected from the group consisting of nucleotide Nos. 85-1032, 7906-8829, 13756-14694, 16917-17862, 21658-22584 and 26413-27336 of SEQ ID NO: 1, and nucleotide Nos. 1648-2673, 6322-7344, 9676-10773, 16543-17565, 21991-23019 and 27367-28392 of SEQ ID NO: 2; or

a DNA which hybridizes with said DNA under stringent conditions and which encodes a polypeptide having acyltransferase activity.

25. A DNA comprising the nucleotide sequence selected from the group consisting of nucleotide Nos. 1096-1353, 5935-6180, 11413-11658, 14902-15147, 19693-19938, 24445-24690 and 30064-30309 of SEQ ID NO: 1, and nucleotide Nos. 4447-4692, 7573-7818, 13378-13659, 20089-20334, 25489-25734 and 30880-31125 of SEQ ID NO: 2; or

a DNA which hybridizes with said DNA under stringent conditions and which encodes a polypeptide having acyl carrier protein activity.

26. A DNA comprising the nucleotide sequence selected from the group consisting of nucleotide Nos. 1441-2742, 6256-7545, 12076-13368, 15217-16506, 20008-21297, and 24781-26079 of SEQ ID NO: 1 and nucleotide Nos. 100-1383,

4771-6060, 7906-9258, 14935-16224, 20413-21705 and 25810-27102 of SEQ ID NO: 1; or

a DNA which hybridizes with said DNA under stringent conditions and which encodes a polypeptide having β-ketoacyl-ACP synthase activity.

27. A DNA comprising the nucleotide sequence selected from the group consisting of nucleotide Nos. 5143-5676, 10609-11142, 18886-19419, 23602-24138 and 29227-29760 of SEQ ID NO: 1, and nucleotide Nos. 3634-4188, 12547-13104, 19285-19842, 24685-25242 and 30076-30633 of SEQ ID NO: 2; or

a DNA which hybridizes with said DNA under stringent conditions and which encodes a polypeptide having β-ketoacyl-ACP reductase activity.

28. A DNA comprising the nucleotide sequence selected from the group consisting of nucleotide Nos. 8947-9384 and 27475-27894 of SEQ ID NO: 1, and nucleotide Nos. 10885-11289, 17689-18066, 23149-23529 and 28516-28878 of SEQ ID NO: 2; or

a DNA which hybridizes with said DNA under stringent conditions and which encodes a polypeptide having dehydratase activity.

29. A DNA comprising the nucleotide sequence of nucleotide Nos. 13879-14619 of SEQ ID NO: 2; or

a DNA which hybridizes with said DNA under stringent conditions and which encodes a polypeptide having thioesterase activity.

30. A DNA comprising the nucleotide sequence shown in SEQ ID NO: 7.

31. A polypeptide encoded by the DNA according to any one of claims 1 to 29.

32. A polypeptide comprising an amino acid sequence according to any one of

SEQ ID NOS: 3 to 6; or

a polypeptide comprising an amino acid sequence wherein one or more amino acids are deleted, replaced or added in the amino acid sequence according to any one of SEQ ID NOS: 3 to 6, and having avermectin aglycon synthase activity.

33. A polypeptide comprising the amino acid sequence selected from the group consisting of amino acid Nos. 29-344, 366-451, 481-914, 1050-1356, 1715-1892, 1979-2060, 2086-2515, 2983-3128, 3537-3714 and 3805-3886 of SEQ ID NO: 3, amino acid Nos. 36-466, 596-908, 978-1059, 1083-1512, 1653-1964, 2306-2483, 2575-2656, 2680-3109, 32030-3538, 3878-4056, 4159-4240, 4271-4703, 4815-5122, 5753-5930 and 6032-6113 of SEQ ID NO: 4, amino acid Nos. 34-461, 550-891, 1212-1396, 1483-1564, 1591-2020, 2108-2448, 2525-2606, 2636-3086, 3226-3591, 3629-3763, 4183-4363, 4460-4553 and 4627-4873 of SEQ ID NO: 5, amino acid Nos. 38-467, 574-914, 956-1081, 1488-1673, 1756-1837, 1864-2294, 2390-2732, 2776-2902, 3288-3473, 3556-3637, 3663-4093, 4182-4523, 4565-4685, 5085-5270 and 5353-5434 of SEQ ID NO: 6; or

a polypeptide comprising an amino acid sequence wherein one or more amino acida are deleted, replaced or added in the amino acid sequence selected above, and having avermectin aglycon synthase domain activity.

34. A recombinant vector comprising the DNA according to any one of claims 1 to 30.

35. A transformant obtainable by introducing the DNA according to any one of claims 1 to 30 or the recombinant vector according to claim 34 into a host cell.

36. The transformant according to claim 35 wherein the host cell is an avermectin-producing bacterial strain.

37. The transformant according to claim 35 or 36 wherein the host cell is *Streptomyces avermitilis* K2038 (FERM BP-2775).

38. A process for producing avermectin aglycon synthase or avermectin aglycon synthase domain polypeptide comprising:
culturing the transformant according to any one of claims 35 to 37 in a medium to produce and accumulate the enzyme or the domain polypeptide in the culture, and
recovering the enzyme or the domain polypeptide from the culture.

39. A process for producing avermectin aglycon or altered avermectin aglycon comprising:

culturing a transformant according to any one of claims 35 to 37 in a medium to produce and accumulate the avermectin aglycon or the altered avermectin aglycon in the culture, and

recovering the avermectin aglycon or the altered avermectin aglycon from the culture.

40. A process for producing avermectin or altered avermectin comprising:
culturing a transformant according to any one of claims 35 to 37 in a medium to produce and accumulate the avermectin aglycon or the altered avermectin aglycon in the culture,
glycosylating the avermectin aglycon or the altered avermectin glycon, and
recovering the resulting avermectin or altered avermectin.

41. The process according to claim 40 wherein altered avermectin is avermectin which has been altered from avermectin B1a to avermectin B2a.

42. An altered avermectin obtainable by the process according to claim 40.

43. An oligonucleotide having a sequence corresponding to 5 to 60 continuous nucleotides in the nucleotide sequence of the DNA according to claim 1 or 2; or an oligonucleotide having a sequence complementary to the oligonucleotide.

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ABSTRACT

The present invention relates to an isolated DNA which comprises a DNA sequence encoding avermectin aglycon synthase domains that corresponds to multifunctional enzyme proteins involved in the biosynthesis of a polyketide compound, or its mutants having avermectin aglycon synthase activity, particularly functional modules and submodules in the DNA sequence derived from *Streptomyces avermitilis*, a polypeptide or mutants thereof encoded by the DNA or the mutants, a vector containing the DNA or the mutants, a host cell transformed with the DNA, the mutants thereof, or the vector, and a method for producing avermectin.

FIG.1

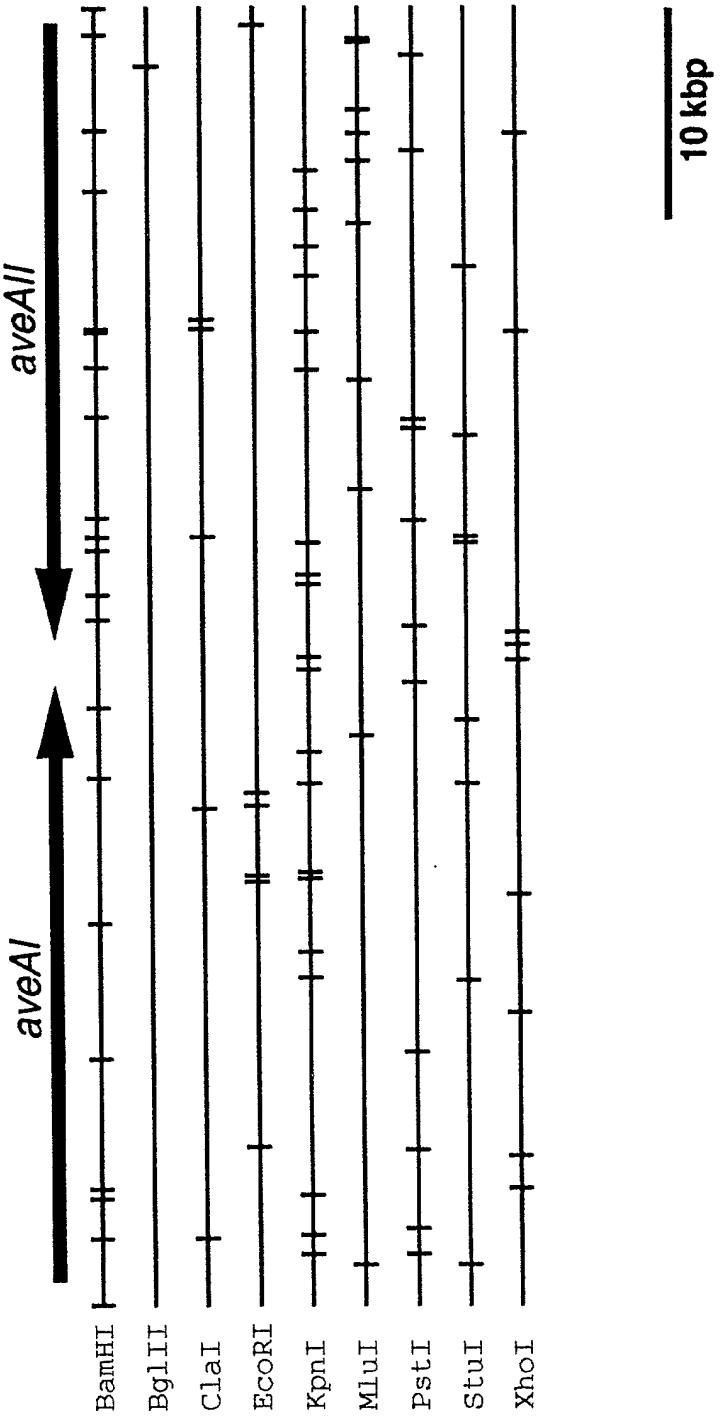

aveAII
aveAI
10 kbp
BamHI
BglII
ClaI
EcoRI
KpnI
MluI
PstI
StuI
XhoI

FIG.2

(1)
(2)
(3)
aveAI
aveC
aveE
aveAII
PKS-1
PKS-2
PKS-3
PKS-4
SU1
SU2
SU3
SU4
SU5
SU6
SU7
SU8
SU9
SU10
SU11
SU12
SU1 (6.09 kbp)
SU2 (5.40 kbp)
SU3 (3.07 kbp)
SU4 (4.72 kbp)
SU5 (4.68 kbp)
SU6 (5.53 bp)
SU7 (4.59 kbp)
SU8 (3.05 kbp)
SU9 (6.71 kbp)
SU10 (5.40 kbp)
SU11 (5.32 kbp)
SU12 (5.31 kbp)
AT ACP KS AT KR ACP
KS AT DH KR ACP
KS AT ACP
KS AT KR ACP
KS AT KR ACP
KS AT DH KR ACP
ACP KR DH AT KS
ACP KR DH AT KS
TE ACP KR DH AT KS
ACP AT KS
ACP KR* AT KS
KS AT ACP KR ACP
KS AT DH KR ACP
KS AT ACP KR ACP
KS AT KR ACP
KS AT KR ACP
KS AT DH KR ACP
ACP KR DH AT KS
ACP KR DH* AT KS
TE ACP KR DH AT KS
ACP AT KS
ACP KR* AT KS
OH
or
HO
OH

Attorneys Docket No.:_____

DECLARATION, POWER OF ATTORNEY AND PETITION

I (We), the undersigned inventor(s), hereby declare that:

My residence, post office address and citizenship are as stated below next to my name,

I (We) believe that I am (we are) the original, first, and joint (sole) inventor(s) of the subject matter which is claimed and for which a patent is sought on the invention entitled

AVERMECTIN AGLYCON SYNTHASE GENES

the specification of which

☐ is attached hereto.

☐ was filed on _____ as

Application Serial No. _____

and amended on _____.

■ was filed as PCT international application

Number PCT/JP00/01041

on February 23, 2000,

and was amended under PCT Article 19

on _____ (if applicable).

I (We) hereby state that I (We) have reviewed and understand the contents of the above-identified specification, including the claims, as amended by any amendment referred to above; that I (We) do not know and do not believe that this invention was ever known or used before my invention or discovery thereof, or patented or described in any printed publication in any country before my invention or discovery thereof, or more than one year prior to this application, or in public use or on sale in the United States for more than one year prior to this application; that this invention or discovery has not been patented or made the subject of an inventor's certificate in any country foreign to the United States on an application filed by me or my legal representatives or assigns more than twelve months before this application.

I (We) acknowledge the duty to disclose information known to be material to the patentability of this application as defined in Section 1.56 of Title 37 Code of Federal Regulations.

I (We) hereby claim foreign priority benefits under Section 119(a)-(d) of Title 35 United States Code, of any foreign application(s) for patent or inventor s certificate listed below and have also identified below any foreign application for patent or inventor s certificate having a filing date before that of the application on which priority is claimed:

Application No.	Country	Filing date	Priority claimed	
46961/1999	Japan	February 24, 1999	■ Yes	☐ No
			☐ Yes	☐ No
			☐ Yes	☐ No
			☐ Yes	☐ No

I hereby claim the benefit under Section 119(e) of Title 35 United States Code, of any United States application(s) listed below.

(Application Number)	(Filing Date)
(Application Number)	(Filing Date)

I (We) hereby claim the benefit under Section 120 of Title 35 United States Code, of any United States application(s) listed below and, insofar as the subject matter of each of the claims of this application is not disclosed in the prior United States application in the manner provided by the first paragraph of Section 112 of Title 35 United States Code, I (We) acknowledge the duty to disclose material information as defined in Section 1.56(a) of Title 37 Code of Federal Regulations, which occurred between the filing date of the prior application and national or PCT international filing date of this application:

Application Serial No.	Filing Date	Status (pending, patented, abandoned)

(24)

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I (We) declare further that all statements made herein of my (our) knowledge are true and that all statements were made with the knowledge that willful false statements and the like so made are punishable by fine or imprisonment, or both, under Section 1001 of Title 18 of the United States Code and that such willful false statements may jeopardize the validity of the application or any patent issued thereon.

1-00

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ctc gcc cac cac cgc cac acc cac cac ctc ccc gcc acc agc atc gcc 5664
Leu Ala His His Arg His Thr His His Leu Pro Ala Thr Ser Ile Ala
1875 1880 1885

tgg ggc acc tgg caa gga aac gga ctc gct gat tcg gac aag gcc cgc 5712
Trp Gly Thr Trp Gln Gly Asn Gly Leu Ala Asp Ser Asp Lys Ala Arg
1890 1895 1900

gca tat ctc gac cgc cgc ggg ttt cga ccc atg tca ccc gag ttg gcc 5760
Ala Tyr Leu Asp Arg Arg Gly Phe Arg Pro Met Ser Pro Glu Leu Ala
1905 1910 1915 1920

acg gca gcg gtc acg cag gcg atc gcg gac acc gaa cgg ccg tat gtc 5808
Thr Ala Ala Val Thr Gln Ala Ile Ala Asp Thr Glu Arg Pro Tyr Val
1925 1930 1935

gtc atc gcc gac atc gac tgg agc aag atc gaa cac acc tct cag acc 5856
Val Ile Ala Asp Ile Asp Trp Ser Lys Ile Glu His Thr Ser Gln Thr
1940 1945 1950

agc gac ctg gtg agc gcg gcc cgg gaa agg gag cca gct gtc cag cgc 5904
Ser Asp Leu Val Ser Ala Ala Arg Glu Arg Glu Pro Ala Val Gln Arg
1955 1960 1965

ccc act cca ccg gcg gag ttg cac aaa acg ctg gcc cat cag acg tcg 5952
Pro Thr Pro Pro Ala Glu Leu His Lys Thr Leu Ala His Gln Thr Ser
1970 1975 1980

gcc gac caa cgg gcc gca ttg ctc gag ctc gta cga gac cat gtg gcg 6000
Ala Asp Gln Arg Ala Ala Leu Leu Glu Leu Val Arg Asp His Val Ala
1985 1990 1995 2000

gca gtg ctc cgg cac gcg gac ccg aaa gcc atc gcg ccc gac cag tcg 6048
Ala Val Leu Arg His Ala Asp Pro Lys Ala Ile Ala Pro Asp Gln Ser
2005 2010 2015

ttc cgt gca ctc ggc ttc gat tca ctc acg gcc gtc gag ttc cga aac 6096
Phe Arg Ala Leu Gly Phe Asp Ser Leu Thr Ala Val Glu Phe Arg Asn
2020 2025 2030

ctg ctg atc aag gca aca gga ctc cgc ctt cct gtc tcg ctg gtc ttc 6144
Leu Leu Ile Lys Ala Thr Gly Leu Arg Leu Pro Val Ser Leu Val Phe
2035 2040 2045

gac cac ccg acc cct gcc aaa ctc gcc gta cac ctg cag aac caa ctg 6192
Asp His Pro Thr Pro Ala Lys Leu Ala Val His Leu Gln Asn Gln Leu
2050 2055 2060

cgg ggc aca gca gcg gag tcg gct cct tca gcg gca gcc gtt acc gcc 6240
Arg Gly Thr Ala Ala Glu Ser Ala Pro Ser Ala Ala Ala Val Thr Ala
2065 2070 2075 2080

gag gct tct gtc acc gag ccg atc gcc atc gtt ggc atg gcc tgt cgt 6288
Glu Ala Ser Val Thr Glu Pro Ile Ala Ile Val Gly Met Ala Cys Arg
2085 2090 2095

ttc ccc ggc gga gtg acc tcg gcg gac gac ttc tgg gat ctg atc tcc 6336
Phe Pro Gly Gly Val Thr Ser Ala Asp Asp Phe Trp Asp Leu Ile Ser
2100 2105 2110

tcc gag cag gac gcg atc ggc gga ttc ccc acc gac cgc ggc tgg gac 6384
Ser Glu Gln Asp Ala Ile Gly Gly Phe Pro Thr Asp Arg Gly Trp Asp
2115 2120 2125

ctg gac acg ctc tac gac ccc gac ccc gac cac ccc ggc acc tgc tac 6432
Leu Asp Thr Leu Tyr Asp Pro Asp Pro Asp His Pro Gly Thr Cys Tyr
2130 2135 2140

acc cga aac ggc gga ttc ctc tac gac gca ggc cac ttc gac gcc gaa 6480

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Thr Arg Asn Gly Gly Phe Leu Tyr Asp Ala Gly His Phe Asp Ala Glu
2145 2150 2155 2160

ttc ttc ggc atc agc ccc cgc gaa gcc ctc gcc atg gac ccc cag caa 6528
Phe Phe Gly Ile Ser Pro Arg Glu Ala Leu Ala Met Asp Pro Gln Gln
2165 2170 2175

cga ctc ctc ctc gaa acc gcc tgg gaa acc atc gaa cac gcc ggc atc 6576
Arg Leu Leu Leu Glu Thr Ala Trp Glu Thr Ile Glu His Ala Gly Ile
2180 2185 2190

aac ccc cac acc ctc cac ggc acc ccc acc gga gtc ttc acc ggc acc 6624
Asn Pro His Thr Leu His Gly Thr Pro Thr Gly Val Phe Thr Gly Thr
2195 2200 2205

aac gga cag gac tac gca ctt cgc gtg cac aac gcg ggc cag tca acc 6672
Asn Gly Gln Asp Tyr Ala Leu Arg Val His Asn Ala Gly Gln Ser Thr
2210 2215 2220

gat ggt ttc gca ctg acc gga acc gcc ggc agc gtc atc tcc ggt cgt 6720
Asp Gly Phe Ala Leu Thr Gly Thr Ala Gly Ser Val Ile Ser Gly Arg
2225 2230 2235 2240

atc tcg tac acg ttt ggt ttt gag ggt cct gcg gtg tcg gtg gac acg 6768
Ile Ser Tyr Thr Phe Gly Phe Glu Gly Pro Ala Val Ser Val Asp Thr
2245 2250 2255

gct tgt tcc tcg tcg ttg gtg gct ttg cat ctg gcc tgt cag gcg ttg 6816
Ala Cys Ser Ser Ser Leu Val Ala Leu His Leu Ala Cys Gln Ala Leu
2260 2265 2270

cgt gcg ggt gag tgc tcg atg gcg ctt gcc ggg ggt gtg acg gtg atg 6864
Arg Ala Gly Glu Cys Ser Met Ala Leu Ala Gly Gly Val Thr Val Met
2275 2280 2285

tcg tct ccg ggt gcc ttc gtg gag ttt tcg cgg cag cgg ggt ctg gcc 6912
Ser Ser Pro Gly Ala Phe Val Glu Phe Ser Arg Gln Arg Gly Leu Ala
2290 2295 2300

gcg gac ggg cat tgc aag gcg ttc tcg gcg gcg gcg gac ggg acc ggc 6960
Ala Asp Gly His Cys Lys Ala Phe Ser Ala Ala Ala Asp Gly Thr Gly
2305 2310 2315 2320

tgg ggt gag ggt gtg ggg atg ctg ctg gtg gag cgg ctc tcc gac gcc 7008
Trp Gly Glu Gly Val Gly Met Leu Leu Val Glu Arg Leu Ser Asp Ala
2325 2330 2335

cat cgc aac ggt cac cgt gtc ctg gcc gtg gtg cgt ggc agt gcg gtc 7056
His Arg Asn Gly His Arg Val Leu Ala Val Val Arg Gly Ser Ala Val
2340 2345 2350

aac cag gac ggt gcg agc aac ggt ctg acc gcg ccc aac ggg ccg tcc 7104
Asn Gln Asp Gly Ala Ser Asn Gly Leu Thr Ala Pro Asn Gly Pro Ser
2355 2360 2365

cag cag cgt gtc atc cgc cag gcc ctc gcc aac gcc ggc ttg tcg gcc 7152
Gln Gln Arg Val Ile Arg Gln Ala Leu Ala Asn Ala Gly Leu Ser Ala
2370 2375 2380

ggt gat gtc gac gcg gtg gag gcc cac ggc acc ggc acc act ttg ggc 7200
Gly Asp Val Asp Ala Val Glu Ala His Gly Thr Gly Thr Thr Leu Gly
2385 2390 2395 2400

gac ccg atc gag gcc cag gcc ctc ctc gcg acc tac gga cag gac cgt 7248
Asp Pro Ile Glu Ala Gln Ala Leu Leu Ala Thr Tyr Gly Gln Asp Arg
2405 2410 2415

gcc ggc gag ggg ccg ctg tgg ctg ggc tcg gtc aag tcc aat gtc ggt 7296
Ala Gly Glu Gly Pro Leu Trp Leu Gly Ser Val Lys Ser Asn Val Gly
2420 2425 2430

cac aca cag gct gcc gcg ggc gtc gcc ggg gtg atc aag atg gtg atg 7344
His Thr Gln Ala Ala Ala Gly Val Ala Gly Val Ile Lys Met Val Met
2435 2440 2445

gcg ctg cgg cat ggt ctg ctg ccg cgg acg ttg cat gtg gat gag ccg 7392

Ala Leu Arg His Gly Leu Leu Pro Arg Thr Leu His Val Asp Glu Pro
2450 2455 2460

tcg ccg cat gtg gac tgg tcc gcg ggt gcg gtg cag ctg ctg acg gag 7440
Ser Pro His Val Asp Trp Ser Ala Gly Ala Val Gln Leu Leu Thr Glu
2465 2470 2475 2480

acg gtg ccc tgg ccc ggc ggg gag ggg cgg cta cgg cgg gca gga gtg 7488
Thr Val Pro Trp Pro Gly Gly Glu Gly Arg Leu Arg Arg Ala Gly Val
2485 2490 2495

tca tca ttc ggc gtc agc ggc acc aac gcc cac gtc atc ctc gaa gaa 7536
Ser Ser Phe Gly Val Ser Gly Thr Asn Ala His Val Ile Leu Glu Glu
2500 2505 2510

gca ccc gcc gac gac gtt ccg ggg gga cca ccc gcc ggc gag ggt gac 7584
Ala Pro Ala Asp Asp Val Pro Gly Gly Pro Pro Ala Gly Glu Gly Asp
2515 2520 2525

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Ala Gly Ser Asp Asp Glu Ala Ala Ala Gly Ser Pro Gly Val Trp Pro
2530 2535 2540

tgg ctg gtg tcg gcc aag tcg cag ccg gcc ctg cgc gcc cag gcc cag 7680
Trp Leu Val Ser Ala Lys Ser Gln Pro Ala Leu Arg Ala Gln Ala Gln
2545 2550 2555 2560

gcc ctg cac gcc cac ctc acc gac cac ccc ggc ctc gac ctc gcg gat 7728
Ala Leu His Ala His Leu Thr Asp His Pro Gly Leu Asp Leu Ala Asp
2565 2570 2575

gtc gga tac acc ctc gcc cac gcc cgc gcc gtg ttc gac cac cgc gcc 7776
Val Gly Tyr Thr Leu Ala His Ala Arg Ala Val Phe Asp His Arg Ala
2580 2585 2590

acc ctc atc gcc gcg gac cgc gac acg ttc ctg caa gca ctc cag gca 7824
Thr Leu Ile Ala Ala Asp Arg Asp Thr Phe Leu Gln Ala Leu Gln Ala
2595 2600 2605

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ctc gcc gca ggc gag ccc cac ccc gcc gtc atc cac agc agc gcc ccg 7872
Leu Ala Ala Gly Glu Pro His Pro Ala Val Ile His Ser Ser Ala Pro
2610 2615 2620

ggc ggg acc ggg acc ggg gag gcc gca gga aag acc gca ttc atc tgc 7920
Gly Gly Thr Gly Thr Gly Glu Ala Ala Gly Lys Thr Ala Phe Ile Cys
2625 2630 2635 2640

tcc gga cag ggc acc caa cgc ccc ggc atg gcc cac ggc ctc tac cac 7968
Ser Gly Gln Gly Thr Gln Arg Pro Gly Met Ala His Gly Leu Tyr His
2645 2650 2655

acc cac ccc gtc ttc gcc gcc gca ctc aac gac atc tgc acc cac ctc 8016
Thr His Pro Val Phe Ala Ala Ala Leu Asn Asp Ile Cys Thr His Leu
2660 2665 2670

gac ccc cac ctc gac cac ccc ctc ctc ccc ctc ctc acc caa aac gac 8064
Asp Pro His Leu Asp His Pro Leu Leu Pro Leu Leu Thr Gln Asn Asp
2675 2680 2685

aac gac aac gag gac gcg gcc gca ctg ctc cag cag acc cgc tac gcc 8112
Asn Asp Asn Glu Asp Ala Ala Ala Leu Leu Gln Gln Thr Arg Tyr Ala
2690 2695 2700

cag ccc gcc ctc ttc gcc ttc cag gtc gcc ctc cac cgc ctc ctc acc 8160
Gln Pro Ala Leu Phe Ala Phe Gln Val Ala Leu His Arg Leu Leu Thr
2705 2710 2715 2720

gac ggc tac cac atc acc ccc cac tac tac gcc gga cac tcc ctc ggc 8208
Asp Gly Tyr His Ile Thr Pro His Tyr Tyr Ala Gly His Ser Leu Gly
2725 2730 2735

gaa atc acc gcc gcc cac ctc gcc ggc atc ctc acc ctc acc gac gcc 8256
Glu Ile Thr Ala Ala His Leu Ala Gly Ile Leu Thr Leu Thr Asp Ala
2740 2745 2750

acc acc ctc atc acc caa cgc gcc acc ctc atg caa acc atg ccc ccc 8304

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Thr Thr Leu Ile Thr Gln Arg Ala Thr Leu Met Gln Thr Met Pro Pro
2755 2760 2765

ggc acc atg acc acc ctc cac acc acc ccc cac cac atc acc cac cac 8352
Gly Thr Met Thr Thr Leu His Thr Thr Pro His His Ile Thr His His
2770 2775 2780

ctc acc gcc cac gaa aac gac ctc gcc atc gcc gcc atc aac acc ccc 8400
Leu Thr Ala His Glu Asn Asp Leu Ala Ile Ala Ala Ile Asn Thr Pro
2785 2790 2795 2800

acc tcc ctc gtc atc agc ggc acc ccc cac acc gtc caa cac atc acc 8448
Thr Ser Leu Val Ile Ser Gly Thr Pro His Thr Val Gln His Ile Thr
2805 2810 2815

acc ctc tgc caa caa caa ggc atc aaa acc aaa acc ctc ccc acc aac 8496
Thr Leu Cys Gln Gln Gln Gly Ile Lys Thr Lys Thr Leu Pro Thr Asn
2820 2825 2830

cac gcc ttc cac tcc ccc cac acc aac ccc atc ctc aac caa ctc cac 8544
His Ala Phe His Ser Pro His Thr Asn Pro Ile Leu Asn Gln Leu His
2835 2840 2845

cag cac acc caa acc ctc acc tac cac cca ccc cac acc ccc ctc atc 8592
Gln His Thr Gln Thr Leu Thr Tyr His Pro Pro His Thr Pro Leu Ile
2850 2855 2860

acc gcc aac acc cca ccc gac caa ctc ctc acc ccc cac tac tgg acc 8640
Thr Ala Asn Thr Pro Pro Asp Gln Leu Leu Thr Pro His Tyr Trp Thr
2865 2870 2875 2880

caa caa gcc cgc aac acc gtc gac tac gcc acc acc acc caa acc ctc 8688
Gln Gln Ala Arg Asn Thr Val Asp Tyr Ala Thr Thr Thr Gln Thr Leu
2885 2890 2895

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His Gln His Gly Val Thr Thr Tyr Ile Glu Leu Gly Pro Asp Asn Thr
2900 2905 2910

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Leu Thr Thr Leu Thr His His Asn Leu Pro Asn Pro Pro Thr Thr Thr
2915 2920 2925

ctc acc ctc acc cac ccc cac cac cac ccc caa acc cac ctc ctc acc 8832
Leu Thr Leu Thr His Pro His His His Pro Gln Thr His Leu Leu Thr
2930 2935 2940

aac ctc gcc aaa acc acc acc acc tgg cac ccc cac cac tac acc cac 8880
Asn Leu Ala Lys Thr Thr Thr Thr Trp His Pro His His Tyr Thr His
2945 2950 2955 2960

cac gac aac caa ccc cac acc cac acc cac ctc gac ctc ccc acc tac 8928
His Asp Asn Gln Pro His Thr His Thr His Leu Asp Leu Pro Thr Tyr
2965 2970 2975

ccc ttc caa cac cac cac tac tgg ctc gaa agc aca cag ccc ggt gcc 8976
Pro Phe Gln His His His Tyr Trp Leu Glu Ser Thr Gln Pro Gly Ala
2980 2985 2990

ggc aac gtg tca gca gcc gga ctc gac ccc acc gaa cac ccc cta ctc 9024
Gly Asn Val Ser Ala Ala Gly Leu Asp Pro Thr Glu His Pro Leu Leu
2995 3000 3005

ggc gcc aca ttg gaa ctg gcg act gac ggt gga gcg ctt ctt gca ggg 9072
Gly Ala Thr Leu Glu Leu Ala Thr Asp Gly Gly Ala Leu Leu Ala Gly
3010 3015 3020

cgc ttg tct ttg agg tcg cat ccg tgg ctg gct gac cat gcc gtc ggc 9120
Arg Leu Ser Leu Arg Ser His Pro Trp Leu Ala Asp His Ala Val Gly
3025 3030 3035 3040

ggc acg gtg ctg ctg tcg ggc gcc acc ttc ctc gaa ctc gcc ctt cat 9168
Gly Thr Val Leu Leu Ser Gly Ala Thr Phe Leu Glu Leu Ala Leu His
3045 3050 3055

gcg ggc aca tac gtg ggc tgc gac cga gtg gat gag ctg acg ctg cat 9216

pct-seq-listing.txt

Footage-08251999

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          3060                3065                3070

gcg ccg ctg gtg gtt cct gtg gat ggg ggt gtg agt gtg cag gtt ggg   9264
Ala Pro Leu Val Val Pro Val Asp Gly Gly Val Ser Val Gln Val Gly
       3075                3080                3085

gtt gcg gct gcg gat ggg gag ggg cgg cgt ttg gtg agt gtg tat gcg   9312
Val Ala Ala Ala Asp Gly Glu Gly Arg Arg Leu Val Ser Val Tyr Ala
   3090                3095                3100

cgg ggt ggg agt gct tgt ggt ggg ggt ggt gcg tcg ggt ggg gtg tgg   9360
Arg Gly Gly Ser Ala Cys Gly Gly Gly Gly Ala Ser Gly Gly Val Trp
3105                3110                3115                3120

acg tgt cat gcc tcg ggg gtg ctg gtt gag gct gct gct ggt ggt gtg   9408
Thr Cys His Ala Ser Gly Val Leu Val Glu Ala Ala Ala Gly Gly Val
               3125                3130                3135

gtg gtg gat ggt ctg gcg ggg gtg tgg ccg ccg cgg ggt gcg gtg gcg   9456
Val Val Asp Gly Leu Ala Gly Val Trp Pro Pro Arg Gly Ala Val Ala
          3140                3145                3150

gtg gat gtc gat ggt gtc cgt gac cgt ttg gct ggg gct ggt tgt gtt   9504
Val Asp Val Asp Gly Val Arg Asp Arg Leu Ala Gly Ala Gly Cys Val
       3155                3160                3165

ttg ggg ccg gtg ttt tcg ggg ctg cgt gcg gtg tgg cgt gat ggg ggg   9552
Leu Gly Pro Val Phe Ser Gly Leu Arg Ala Val Trp Arg Asp Gly Gly
   3170                3175                3180

gat ttg ctg gct gag gtg tgt ctg ccg gag gag gcg tgg ggt gat gcg   9600
Asp Leu Leu Ala Glu Val Cys Leu Pro Glu Glu Ala Trp Gly Asp Ala
3185                3190                3195                3200

gct ggt ttt ggg ctg cat ccg gcg ttg ctg gat ggt gtg gtc cag ccg   9648
Ala Gly Phe Gly Leu His Pro Ala Leu Leu Asp Gly Val Val Gln Pro
               3205                3210                3215
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ttg tcg gtg ttg ctt ccg ggt ggg acg ggg ttt ggg gag ggg gcg ggg 9696
Leu Ser Val Leu Leu Pro Gly Gly Thr Gly Phe Gly Glu Gly Ala Gly
3220 3225 3230

ttc ggg gag ggt gtt cgg gtg ccg gct gtg tgg ggt ggt gtg tcg ctt 9744
Phe Gly Glu Gly Val Arg Val Pro Ala Val Trp Gly Gly Val Ser Leu
3235 3240 3245

cac cgg gcg ggt gtg acc ggt gtg cgg gtg cgt gtg tcg gct gtc ggg 9792
His Arg Ala Gly Val Thr Gly Val Arg Val Arg Val Ser Ala Val Gly
3250 3255 3260

cgg ggc ggc ggg cgt gag gcg gtg tcg gtc gtg gtc ggg gat gag gcg 9840
Arg Gly Gly Gly Arg Glu Ala Val Ser Val Val Val Gly Asp Glu Ala
3265 3270 3275 3280

ggt gtg ccg gtg gcg tcg gtc gat cgt ctt gag ttg cgg cct gtg gat 9888
Gly Val Pro Val Ala Ser Val Asp Arg Leu Glu Leu Arg Pro Val Asp
3285 3290 3295

atg ggt cag ttg cgt gct gtc tcg gtt tcg gcg ggg cgg cgg ggt tcg 9936
Met Gly Gln Leu Arg Ala Val Ser Val Ser Ala Gly Arg Arg Gly Ser
3300 3305 3310

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Leu Tyr Ala Val Gln Trp Ala Glu Val Gly Pro Val Pro Val Cys Gly
3315 3320 3325

cag gcg tgg gcg tgg cac gag gac gtg ggt gag agc ggt ggt ggg cct 10032
Gln Ala Trp Ala Trp His Glu Asp Val Gly Glu Ser Gly Gly Gly Pro
3330 3335 3340

gtg ccg ggg gtg gtg gtg ttg cgg tgc ccg gat gcc ggt gcc ggt ggc 10080
Val Pro Gly Val Val Val Leu Arg Cys Pro Asp Ala Gly Ala Gly Gly
3345 3350 3355 3360

ggt ggc ggt ggc ggt ggt ggc ggt ggt gtg ggt gag gtt gtt ggt ggg 10128

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Gly Gly Gly Gly Gly Gly Gly Gly Gly Val Gly Glu Val Val Gly Gly
3365 3370 3375

gtg ttg ggt gtg gtg cag ggg tgg ctg ggg ctg gag cgg ttt gcg ggt 10176
Val Leu Gly Val Val Gln Gly Trp Leu Gly Leu Glu Arg Phe Ala Gly
3380 3385 3390

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Ser Arg Leu Val Val Val Thr Arg Gly Ala Val Val Ala Gly Pro Glu
3395 3400 3405

gac ggc ccg gtg gat gtg gtg ggt gcg tcg gtg tgg ggg ctg gtg cgt 10272
Asp Gly Pro Val Asp Val Val Gly Ala Ser Val Trp Gly Leu Val Arg
3410 3415 3420

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Ser Ala Gln Ala Glu His Pro Asp Arg Phe Val Leu Leu Asp Leu Asp
3425 3430 3435 3440

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Thr Asp Thr Gly Thr Asp Leu Asp Thr Gly Ala Gly Ala Gly Trp Gly
3445 3450 3455

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Val Asp Gly Gly Arg Val Ala Ala Val Val Ala Cys Gly Glu Pro Gln
3460 3465 3470

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Leu Ala Val Arg Gly Glu Arg Leu Leu Ala Ala Arg Leu Lys Arg Leu
3475 3480 3485

gag tca tcc ggt gat gtt cca gcc cag cgg tcc ggt gac aca cga gcc 10512
Glu Ser Ser Gly Asp Val Pro Ala Gln Arg Ser Gly Asp Thr Arg Ala
3490 3495 3500

cgg cgg tcc gac gtg cct gcc cag cgc tcc ggt ggc gtg cct gct cgg 10560
Arg Arg Ser Asp Val Pro Ala Gln Arg Ser Gly Gly Val Pro Ala Arg
3505 3510 3515 3520

WO 2004/094595 PCT/US2004/012101

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Arg Ser Val Asp Val Ser Gly Arg Glu Val Leu Pro Trp Leu Ser Gly
3525 3530 3535

ggg tcg gtg ttg gtg acg ggt ggg acg ggt gtg ctg ggt gcg gcg gtg 10656
Gly Ser Val Leu Val Thr Gly Gly Thr Gly Val Leu Gly Ala Ala Val
3540 3545 3550

gcg cgg cat ctg gct ggt gtg tgt ggg gtg cgg gat ctg ctg ttg gtg 10704
Ala Arg His Leu Ala Gly Val Cys Gly Val Arg Asp Leu Leu Leu Val
3555 3560 3565

agc cgg cgt ggt ccg gat gct ccg ggt gcg gag ggt ctg cgg gcg gag 10752
Ser Arg Arg Gly Pro Asp Ala Pro Gly Ala Glu Gly Leu Arg Ala Glu
3570 3575 3580

ctg gcc gcg ttg ggg gcg gag gtg cgg att gtt gcg tgt gat gtg ggg 10800
Leu Ala Ala Leu Gly Ala Glu Val Arg Ile Val Ala Cys Asp Val Gly
3585 3590 3595 3600

gag cgg cgg gag gtg gtc cgg ctg ctg gag ggt gtt cct gcc ggg tgt 10848
Glu Arg Arg Glu Val Val Arg Leu Leu Glu Gly Val Pro Ala Gly Cys
3605 3610 3615

ccg ctg acg ggt gtc gtg cat gcg gct ggt gtg ctg gac gat gcg acg 10896
Pro Leu Thr Gly Val Val His Ala Ala Gly Val Leu Asp Asp Ala Thr
3620 3625 3630

atc gcc tct ctc acg ccc gag cgg ctg ggc acg gtg ttc gcg gcc aag 10944
Ile Ala Ser Leu Thr Pro Glu Arg Leu Gly Thr Val Phe Ala Ala Lys
3635 3640 3645

gtg gat gcc gct ctt ttg ctg gat gag ctg acg cgg ggt atg gag ctg 10992
Val Asp Ala Ala Leu Leu Leu Asp Glu Leu Thr Arg Gly Met Glu Leu
3650 3655 3660

tcg gcg ttc gtg ctg ttc tcc tcg gcc gcg ggg atc ctg ggg tcg gcc 11040

Ser Ala Phe Val Leu Phe Ser Ser Ala Ala Gly Ile Leu Gly Ser Ala
3665 3670 3675 3680

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Gly Gln Gly Asn Tyr Ala Ala Ala Asn Ala Ala Leu Asp Ala Leu Ala
3685 3690 3695

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Tyr Arg Arg Arg Ala Ala Gly Leu Pro Gly Val Ser Leu Ala Trp Gly
3700 3705 3710

ctg tgg gaa gag gcc agc ggg atg acc ggg cac ctg gcc ggc acc gac 11184
Leu Trp Glu Glu Ala Ser Gly Met Thr Gly His Leu Ala Gly Thr Asp
3715 3720 3725

cac cgg cgc atc atc cgt tcc ggt ctg cat ccc atg tcg acc ccg gac 11232
His Arg Arg Ile Ile Arg Ser Gly Leu His Pro Met Ser Thr Pro Asp
3730 3735 3740

gca ctg gcc ctc ttc gat gcg gcc ctg gct ctg gac cgg ccg gtc ctg 11280
Ala Leu Ala Leu Phe Asp Ala Ala Leu Ala Leu Asp Arg Pro Val Leu
3745 3750 3755 3760

ctg ccc gcc gac ctg cgt ccc gcc ccg ccc ctg ccg ccc ctg ctg cag 11328
Leu Pro Ala Asp Leu Arg Pro Ala Pro Pro Leu Pro Pro Leu Leu Gln
3765 3770 3775

gac ctc ctg ccc gcc acc cgc cgc cgc acc acc cgc acc acc act acc 11376
Asp Leu Leu Pro Ala Thr Arg Arg Arg Thr Thr Arg Thr Thr Thr Thr
3780 3785 3790

ggt ggt gcg gac aac ggc gcc cag ctg cac gcc cgg ctg gcc ggc cag 11424
Gly Gly Ala Asp Asn Gly Ala Gln Leu His Ala Arg Leu Ala Gly Gln
3795 3800 3805

aca cac gaa caa cag cac acc acc ctc ctc gcc ctg gtc cgc tcc cac 11472
Thr His Glu Gln Gln His Thr Thr Leu Leu Ala Leu Val Arg Ser His
3810 3815 3820

WO 2004/063351 PCT/US2003/040410

atc gcc acc gtc ctg ggc cac acc acc ccc gac acc atc ccc ccc gac 11520
Ile Ala Thr Val Leu Gly His Thr Thr Pro Asp Thr Ile Pro Pro Asp
3825 3830 3835 3840

cgc gcg ttc cgc gac ctc ggc ttc gac tcc ctc acc gcc gtc gaa cta 11568
Arg Ala Phe Arg Asp Leu Gly Phe Asp Ser Leu Thr Ala Val Glu Leu
3845 3850 3855

cgc aac cgg ctc tcc cgc acc acc gga ctc cgc ctc ccc acc acc ctc 11616
Arg Asn Arg Leu Ser Arg Thr Thr Gly Leu Arg Leu Pro Thr Thr Leu
3860 3865 3870

gcc ttc gac cac ccc aac ccc acc acc ctc acc cac cac ctc cac aca 11664
Ala Phe Asp His Pro Asn Pro Thr Thr Leu Thr His His Leu His Thr
3875 3880 3885

caa ctc cag cca caa ccg gac aac gct gtc gcc ccc gtg ttg gcg gag 11712
Gln Leu Gln Pro Gln Pro Asp Asn Ala Val Ala Pro Val Leu Ala Glu
3890 3895 3900

ctc gac aaa ctc gaa tcc gcc ctc tcc gcc ctc gac aaa acc gac agc 11760
Leu Asp Lys Leu Glu Ser Ala Leu Ser Ala Leu Asp Lys Thr Asp Ser
3905 3910 3915 3920

gcc agc gaa aga gtc acc ctg cgg ctg aag tca ctc atg ttg agg tgg 11808
Ala Ser Glu Arg Val Thr Leu Arg Leu Lys Ser Leu Met Leu Arg Trp
3925 3930 3935

aac gca ccc cag cat ccg aca gcc gaa agc gct gat gac gac gag aag 11856
Asn Ala Pro Gln His Pro Thr Ala Glu Ser Ala Asp Asp Asp Glu Lys
3940 3945 3950

ttc aca tcg gca aca gag gct gag att ttc aaa ttc att gac aac gac 11904
Phe Thr Ser Ala Thr Glu Ala Glu Ile Phe Lys Phe Ile Asp Asn Asp
3955 3960 3965

ctc ggc ctg tcc tgaaccggac gcctgccact ccgcccgtat ccgctgggcc 11956

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Leu Gly Leu Ser
3970

ctgctaggac gtga atg caa ttg gcg aat gaa gcg aag ctc ctg gaa tac 12006
Met Gln Leu Ala Asn Glu Ala Lys Leu Leu Glu Tyr
3975 3980

ctc aag cgc gtc act gcg gac ctg gac cgc act cgc cgt cgc ctg tac 12054
Leu Lys Arg Val Thr Ala Asp Leu Asp Arg Thr Arg Arg Arg Leu Tyr
3985 3990 3995 4000

gag gtg gtc gag cgt gag cag gag ccg atc gcg att gtg ggg atg gcg 12102
Glu Val Val Glu Arg Glu Gln Glu Pro Ile Ala Ile Val Gly Met Ala
4005 4010 4015

tgt cgt tac cca ggc ggg gcg acg tca ccc acg cga ctg tgg cat ctc 12150
Cys Arg Tyr Pro Gly Gly Ala Thr Ser Pro Thr Arg Leu Trp His Leu
4020 4025 4030

gtc aag tcc cag acg gac gct atc ggg gag ttc ccg acc gac cgt gga 12198
Val Lys Ser Gln Thr Asp Ala Ile Gly Glu Phe Pro Thr Asp Arg Gly
4035 4040 4045

tgg aac ctg gag cag ctc tac gac ccg gac ccc gac cgc tca gga acc 12246
Trp Asn Leu Glu Gln Leu Tyr Asp Pro Asp Pro Asp Arg Ser Gly Thr
4050 4055 4060

agt tac acg cgc agc gga ggg ttt ctc tat gac gcg ggc gac ttc gac 12294
Ser Tyr Thr Arg Ser Gly Gly Phe Leu Tyr Asp Ala Gly Asp Phe Asp
4065 4070 4075 4080

gcc gcg ttc ttc gag ttg tca ccg cgt gag gcg ctg gca atg gac ccg 12342
Ala Ala Phe Phe Glu Leu Ser Pro Arg Glu Ala Leu Ala Met Asp Pro
4085 4090 4095

cag cag cgc ctg ctg ctc gaa acc act tgg gaa acg ttc gaa cag ggc 12390
Gln Gln Arg Leu Leu Leu Glu Thr Thr Trp Glu Thr Phe Glu Gln Gly
4100 4105 4110

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gga atc gac ccg agg tcc atg cgc gga agc cgg acc ggg gtt ttc gtg 12438
Gly Ile Asp Pro Arg Ser Met Arg Gly Ser Arg Thr Gly Val Phe Val
4115 4120 4125

ggg atc aat ccg gag gac tac acc acc gga tac aca cat cag ccc tca 12486
Gly Ile Asn Pro Glu Asp Tyr Thr Thr Gly Tyr Thr His Gln Pro Ser
4130 4135 4140

aac gca gtc gag ggc tac ctg ctc act ggc agc gcg gca agc att gcg 12534
Asn Ala Val Glu Gly Tyr Leu Leu Thr Gly Ser Ala Ala Ser Ile Ala
4145 4150 4155 4160

tca ggc cgt atc tcc tac aac ttc ggg ctc gaa ggc cct gcg atc act 12582
Ser Gly Arg Ile Ser Tyr Asn Phe Gly Leu Glu Gly Pro Ala Ile Thr
4165 4170 4175

atc gac acc gcg tgt tcc tcc tcg ctc gtc gcc ctg cat ctg gcc tgc 12630
Ile Asp Thr Ala Cys Ser Ser Ser Leu Val Ala Leu His Leu Ala Cys
4180 4185 4190

caa gcg ctc cgg tcc ggt gaa tgc acc atg gcg ctc gca ggc ggc gcc 12678
Gln Ala Leu Arg Ser Gly Glu Cys Thr Met Ala Leu Ala Gly Gly Ala
4195 4200 4205

tcc gtc atg gcc act ccc ttc gtc ttc acc gag ttc tct cgc cag cgg 12726
Ser Val Met Ala Thr Pro Phe Val Phe Thr Glu Phe Ser Arg Gln Arg
4210 4215 4220

ggc ctg gcc gca gac ggc cgg tgc aag gcg ttt tcg gcg gcg gcg gac 12774
Gly Leu Ala Ala Asp Gly Arg Cys Lys Ala Phe Ser Ala Ala Ala Asp
4225 4230 4235 4240

ggg acc ggc tgg tcc gag ggt gtg ggg atg ctg ctg gtg gag cgg ctc 12822
Gly Thr Gly Trp Ser Glu Gly Val Gly Met Leu Leu Val Glu Arg Leu
4245 4250 4255

tcc gac gcc cgc cgc aac ggt cac cgt gtc ctg gcc gtc gtc cgc ggc 12870

Ser Asp Ala Arg Arg Asn Gly His Arg Val Leu Ala Val Val Arg Gly
4260 4265 4270

agc gcc gtc aac cag gac ggc gca agc aac ggc ctg acc gca ccc aac 12918
Ser Ala Val Asn Gln Asp Gly Ala Ser Asn Gly Leu Thr Ala Pro Asn
4275 4280 4285

ggt cgt tca caa gtc aag gtc atc cgc cag gct ttg gcc aac gca cac 12966
Gly Arg Ser Gln Val Lys Val Ile Arg Gln Ala Leu Ala Asn Ala His
4290 4295 4300

ctc tcc cct gcc gat gtc gat gcg gtg gag gcc cac ggc acg ggg acc 13014
Leu Ser Pro Ala Asp Val Asp Ala Val Glu Ala His Gly Thr Gly Thr
4305 4310 4315 4320

acc ctg ggc gac ccg atc gag gct caa gcc ctc gtc gaa gcc tac ggt 13062
Thr Leu Gly Asp Pro Ile Glu Ala Gln Ala Leu Val Glu Ala Tyr Gly
4325 4330 4335

cag gac cgc ccc aac ggc cgc ccc ctc tgg ctc gga acc ctc aag tcc 13110
Gln Asp Arg Pro Asn Gly Arg Pro Leu Trp Leu Gly Thr Leu Lys Ser
4340 4345 4350

aac atc ggg cac tcc atg gcc gct gcg ggt gtg ggc ggg gtc atc aag 13158
Asn Ile Gly His Ser Met Ala Ala Ala Gly Val Gly Gly Val Ile Lys
4355 4360 4365

atg gtg atg gcg ctg cgg aat ggt ctg ctg ccg cgg acg ttg cat gtg 13206
Met Val Met Ala Leu Arg Asn Gly Leu Leu Pro Arg Thr Leu His Val
4370 4375 4380

gat gag ccg tcg ccg cat gtg gac tgg tcc gcg ggt gcg gtg cag ctg 13254
Asp Glu Pro Ser Pro His Val Asp Trp Ser Ala Gly Ala Val Gln Leu
4385 4390 4395 4400

ctg acg gag acg gtg ccc tgg ccc ggc ggg gag ggg cgg cta cgg cgg 13302
Leu Thr Glu Thr Val Pro Trp Pro Gly Gly Glu Gly Arg Leu Arg Arg
4405 4410 4415

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gca gga gtg tca tca ttc ggc gtc agc ggc acc aac gcc cac gtc atc 13350
Ala Gly Val Ser Ser Phe Gly Val Ser Gly Thr Asn Ala His Val Ile
4420 4425 4430

ctc gag gaa gca ccc gcc cac aac atc ccg tca gac aca ccc gcc gac 13398
Leu Glu Glu Ala Pro Ala His Asn Ile Pro Ser Asp Thr Pro Ala Asp
4435 4440 4445

gac gtc ccg gga gaa tca gcc gcc gac gag gat gcc ggt agt ggc gat 13446
Asp Val Pro Gly Glu Ser Ala Ala Asp Glu Asp Ala Gly Ser Gly Asp
4450 4455 4460

gag gct gct gcc ggc agt cca ggg gtg tgg ccg tgg ctg gtg tcg gcc 13494
Glu Ala Ala Ala Gly Ser Pro Gly Val Trp Pro Trp Leu Val Ser Ala
4465 4470 4475 4480

aag tcg cag ccg gcc ctg cgc gcc cag gcc cag gcc ctg cac gcc cac 13542
Lys Ser Gln Pro Ala Leu Arg Ala Gln Ala Gln Ala Leu His Ala His
4485 4490 4495

ctc acc gac cac ccc ggc ctc gac ctc gcc gac gtc ggg tac acc ctc 13590
Leu Thr Asp His Pro Gly Leu Asp Leu Ala Asp Val Gly Tyr Thr Leu
4500 4505 4510

gcc cac gcc cgc gcc gtg ttc gac cac cgc gcc acc ctc atc gcc gcc 13638
Ala His Ala Arg Ala Val Phe Asp His Arg Ala Thr Leu Ile Ala Ala
4515 4520 4525

gac cgc gac acc ttc ctg caa gca ctc cag gca ctc gcc gca ggc gaa 13686
Asp Arg Asp Thr Phe Leu Gln Ala Leu Gln Ala Leu Ala Ala Gly Glu
4530 4535 4540

ccc cac ccc gcc gtc atc cac agc agc gcc cca ggc ggg acc ggg acc 13734
Pro His Pro Ala Val Ile His Ser Ser Ala Pro Gly Gly Thr Gly Thr
4545 4550 4555 4560

ggg gag gcc gca gga aag acc gca ttc atc tgc tcc gga cag ggc acc 13782

Gly Glu Ala Ala Gly Lys Thr Ala Phe Ile Cys Ser Gly Gln Gly Thr
4565 4570 4575

caa cgc ccc ggc atg gcc cac ggc ctc tac cac acc cac ccc gtc ttc 13830
Gln Arg Pro Gly Met Ala His Gly Leu Tyr His Thr His Pro Val Phe
4580 4585 4590

gcc gcc gca ctc aac gac atc tgc acc cac ctc gac ccc cac ctc gac 13878
Ala Ala Ala Leu Asn Asp Ile Cys Thr His Leu Asp Pro His Leu Asp
4595 4600 4605

cac ccc ctc ctc ccc ctc ctc acc cag gac ccc aac acc cag gac acc 13926
His Pro Leu Leu Pro Leu Leu Thr Gln Asp Pro Asn Thr Gln Asp Thr
4610 4615 4620

acc acc ctc gaa gaa gcg gcc gca ctg ctc cag cag acc cgc tac gcc 13974
Thr Thr Leu Glu Glu Ala Ala Ala Leu Leu Gln Gln Thr Arg Tyr Ala
4625 4630 4635 4640

cag ccc gcc ctc ttc gcc ttc cag gtc gcc ctc cac cgc ctc ctc acc 14022
Gln Pro Ala Leu Phe Ala Phe Gln Val Ala Leu His Arg Leu Leu Thr
4645 4650 4655

gac ggc tac cac atc acc ccc cac tac tac gcc gga cac tcc ctc ggc 14070
Asp Gly Tyr His Ile Thr Pro His Tyr Tyr Ala Gly His Ser Leu Gly
4660 4665 4670

gaa atc acc gcc gcc cac ctc gcc ggc atc ctc acc ctc acc gac gcc 14118
Glu Ile Thr Ala Ala His Leu Ala Gly Ile Leu Thr Leu Thr Asp Ala
4675 4680 4685

acc acc ctc atc acc caa cgc gcc acc ctc atg caa acc atg ccc ccc 14166
Thr Thr Leu Ile Thr Gln Arg Ala Thr Leu Met Gln Thr Met Pro Pro
4690 4695 4700

ggc acc atg acc acc ctc cac acc acc ccc cac cac atc acc cac cac 14214
Gly Thr Met Thr Thr Leu His Thr Thr Pro His His Ile Thr His His
4705 4710 4715 4720

ctc acc gcc cac gaa aac gac ctc gcc atc gcc gcc atc aac acc ccc 14262
Leu Thr Ala His Glu Asn Asp Leu Ala Ile Ala Ala Ile Asn Thr Pro
4725 4730 4735

acc tcc ctc gtc atc agc ggc acc ccc cac acc gtc caa cac atc acc 14310
Thr Ser Leu Val Ile Ser Gly Thr Pro His Thr Val Gln His Ile Thr
4740 4745 4750

acc ctc tgc caa caa caa ggc atc aaa acc aaa acc ctc ccc acc aac 14358
Thr Leu Cys Gln Gln Gln Gly Ile Lys Thr Lys Thr Leu Pro Thr Asn
4755 4760 4765

cac gcc ttc cac tcc ccc cac acc aac ccc atc ctc aac caa ctc cac 14406
His Ala Phe His Ser Pro His Thr Asn Pro Ile Leu Asn Gln Leu His
4770 4775 4780

cag cac acc caa acc ctc acc tac cac cca ccc cac acc ccc ctc atc 14454
Gln His Thr Gln Thr Leu Thr Tyr His Pro Pro His Thr Pro Leu Ile
4785 4790 4795 4800

acc gcc aac acc cca ccc gac caa ctc ctc acc ccc cac tac tgg acc 14502
Thr Ala Asn Thr Pro Pro Asp Gln Leu Leu Thr Pro His Tyr Trp Thr
4805 4810 4815

caa caa gcc cgc aac acc gtc gac tac gcc acc acc acc caa acc ctc 14550
Gln Gln Ala Arg Asn Thr Val Asp Tyr Ala Thr Thr Thr Gln Thr Leu
4820 4825 4830

cac caa cac ggc gtc acc acc tac atc gaa ctc gga ccc gac aac acc 14598
His Gln His Gly Val Thr Thr Tyr Ile Glu Leu Gly Pro Asp Asn Thr
4835 4840 4845

ctc acc acc ctc acc cac gac aac ctc ccc aac acc ccc acc acc acc 14646
Leu Thr Thr Leu Thr His Asp Asn Leu Pro Asn Thr Pro Thr Thr Thr
4850 4855 4860

ctc acc ctc acc cac ccc cac cac cac ccc caa acc cac ctc ctc acc 14694

Leu Thr Leu Thr His Pro His His His Pro Gln Thr His Leu Leu Thr
4865 4870 4875 4880

aac ctc gcc aaa acc acc acc acc tgg cac ccc cac cac tac acc cac 14742
Asn Leu Ala Lys Thr Thr Thr Thr Trp His Pro His His Tyr Thr His
4885 4890 4895

cac cac aac caa ccc cac acc cac acc cac ctc gac ctc ccc acc tac 14790
His His Asn Gln Pro His Thr His Thr His Leu Asp Leu Pro Thr Tyr
4900 4905 4910

ccc ttc caa cac cac cac tac tgg ctc caa cca ccc ggc aag ccg agc 14838
Pro Phe Gln His His His Tyr Trp Leu Gln Pro Pro Gly Lys Pro Ser
4915 4920 4925

gac ccg tca ccg agc gaa ggc cgt gag caa gcc acg acc cca tca acc 14886
Asp Pro Ser Pro Ser Glu Gly Arg Glu Gln Ala Thr Thr Pro Ser Thr
4930 4935 4940

ccg ctg cgt gat gtc ctc gtg ggc aag tct ccg cag gag cga gac gaa 14934
Pro Leu Arg Asp Val Leu Val Gly Lys Ser Pro Gln Glu Arg Asp Glu
4945 4950 4955 4960

gag ctg ttg cgc ctg gtg cgc acc cat gcg gcc gct gtg ctg ggc cat 14982
Glu Leu Leu Arg Leu Val Arg Thr His Ala Ala Ala Val Leu Gly His
4965 4970 4975

gcc act ccc gaa gtg atc gtt ccg aac aag gcc ttc aaa gag ctg ggt 15030
Ala Thr Pro Glu Val Ile Val Pro Asn Lys Ala Phe Lys Glu Leu Gly
4980 4985 4990

ttt gat tct ctc gcc gca att cag ctt cgt aat cga ctg ctt gct gac 15078
Phe Asp Ser Leu Ala Ala Ile Gln Leu Arg Asn Arg Leu Leu Ala Asp
4995 5000 5005

gtt gac ctg ccg ctt ccg gcc acg ctg atc ttc gat tac ccc act ccg 15126
Val Asp Leu Pro Leu Pro Ala Thr Leu Ile Phe Asp Tyr Pro Thr Pro
5010 5015 5020

atg gcg ctt tgc cag ttc ctc cgg gcg gcg atc gtc gga gcg gac aca 15174
Met Ala Leu Cys Gln Phe Leu Arg Ala Ala Ile Val Gly Ala Asp Thr
5025 5030 5035 5040

ggc acg acc act cgt ctg ccg cta act gcg gtc ccc gcc gac gag ccg 15222
Gly Thr Thr Thr Arg Leu Pro Leu Thr Ala Val Pro Ala Asp Glu Pro
5045 5050 5055

atc gcc atc gtc ggc atg gcc tgt cgg tac ccc ggt gat gta cgg acg 15270
Ile Ala Ile Val Gly Met Ala Cys Arg Tyr Pro Gly Asp Val Arg Thr
5060 5065 5070

gtc gat gat ctc tgg cag gtg gtc agt ggt ggc cat gac gcg atc ggc 15318
Val Asp Asp Leu Trp Gln Val Val Ser Gly Gly His Asp Ala Ile Gly
5075 5080 5085

gga ttc ccg acg aac cgt ggg tgg gac ctc gac acg ctg tac aac ccg 15366
Gly Phe Pro Thr Asn Arg Gly Trp Asp Leu Asp Thr Leu Tyr Asn Pro
5090 5095 5100

gac ccg gac cac cac gga acc agc tac acc cgg agc ggc gga ttc ctt 15414
Asp Pro Asp His His Gly Thr Ser Tyr Thr Arg Ser Gly Gly Phe Leu
5105 5110 5115 5120

tac gac gca ggc aat ttc gat ccc gac ttc ttc ggt atc agt ccg cgt 15462
Tyr Asp Ala Gly Asn Phe Asp Pro Asp Phe Phe Gly Ile Ser Pro Arg
5125 5130 5135

gag gca ctg gcg atg gac ccg cag cag cgg ctg ctg ctg gaa aca gcg 15510
Glu Ala Leu Ala Met Asp Pro Gln Gln Arg Leu Leu Leu Glu Thr Ala
5140 5145 5150

tgg gag agc atc gaa cac gcc tgc atc aac ccc gac agc ctc cgt ggc 15558
Trp Glu Ser Ile Glu His Ala Cys Ile Asn Pro Asp Ser Leu Arg Gly
5155 5160 5165

aca cca acc ggc gtc ttc gcc ggg ctg acc tac cac gac tac gcc gcg 15606

Thr Pro Thr Gly Val Phe Ala Gly Leu Thr Tyr His Asp Tyr Ala Ala
5170 5175 5180

cgc ttt ccc aca gct ccg gca ggg ttc gag ggg tat ctc ggg cac gga 15654
Arg Phe Pro Thr Ala Pro Ala Gly Phe Glu Gly Tyr Leu Gly His Gly
5185 5190 5195 5200

agc gca ggc agt atc gcc tcg ggt cgt gtc gcc tac gct ctc ggc ctg 15702
Ser Ala Gly Ser Ile Ala Ser Gly Arg Val Ala Tyr Ala Leu Gly Leu
5205 5210 5215

gaa ggt ccg gcc ctc aca gtc gac act gcc tgc tct tcg tcc ctg gtc 15750
Glu Gly Pro Ala Leu Thr Val Asp Thr Ala Cys Ser Ser Ser Leu Val
5220 5225 5230

gct ctg cac ctg gcc tgt cag gcg ctg cgg tcc ggc gag tgt tcc atg 15798
Ala Leu His Leu Ala Cys Gln Ala Leu Arg Ser Gly Glu Cys Ser Met
5235 5240 5245

gcc ctc gcg ggt ggc gtc acg gtg atg tca acc ccg gcc ggg ttc gtg 15846
Ala Leu Ala Gly Gly Val Thr Val Met Ser Thr Pro Ala Gly Phe Val
5250 5255 5260

gag ttt tcg cgg cag cgg ggc ctg gcc gtg gac ggg cgg tgc aag gcg 15894
Glu Phe Ser Arg Gln Arg Gly Leu Ala Val Asp Gly Arg Cys Lys Ala
5265 5270 5275 5280

ttc tcg gca gcg gct gac ggc acc ggc tgg ggt gag ggt gtc gga atg 15942
Phe Ser Ala Ala Ala Asp Gly Thr Gly Trp Gly Glu Gly Val Gly Met
5285 5290 5295

ctg ctg gtg gag cgg ctg tcg gac gcg cgg cgg ctc ggt cac cga atc 15990
Leu Leu Val Glu Arg Leu Ser Asp Ala Arg Arg Leu Gly His Arg Ile
5300 5305 5310

ctc gcg gtg gtg cgt ggc agt gcg gtc aat cag gac ggt gcg agc aac 16038
Leu Ala Val Val Arg Gly Ser Ala Val Asn Gln Asp Gly Ala Ser Asn
5315 5320 5325

ggg ctg acg gcg ccc aac ggg ccg tcc cag gag cgt gtc atc cgc ctg 16086
Gly Leu Thr Ala Pro Asn Gly Pro Ser Gln Glu Arg Val Ile Arg Leu
5330 5335 5340

gcc ctg gcc aac gcg gac ctg acc ccc gcc gac gtc gat gcg gtg gag 16134
Ala Leu Ala Asn Ala Asp Leu Thr Pro Ala Asp Val Asp Ala Val Glu
5345 5350 5355 5360

gcc cac ggc acc ggc acc act ttg ggc gac ccg atc gag gcc cag gcc 16182
Ala His Gly Thr Gly Thr Thr Leu Gly Asp Pro Ile Glu Ala Gln Ala
5365 5370 5375

ctc ctc gcc acc tac gga cag gac cgc ccc ggc aac gaa ccg ctg tgg 16230
Leu Leu Ala Thr Tyr Gly Gln Asp Arg Pro Gly Asn Glu Pro Leu Trp
5380 5385 5390

ctg ggc tcg atg aag tcg aac atc ggc cac gcg cag gct gcc gca ggt 16278
Leu Gly Ser Met Lys Ser Asn Ile Gly His Ala Gln Ala Ala Ala Gly
5395 5400 5405

gtg ggc ggg gtc atc aag atg gtg atg gcg ctg cgg aat ggt ctg ctg 16326
Val Gly Gly Val Ile Lys Met Val Met Ala Leu Arg Asn Gly Leu Leu
5410 5415 5420

ccg cgg acg ttg cat gtg gat gag ccg tcg ccg cat gtg gac tgg tcc 16374
Pro Arg Thr Leu His Val Asp Glu Pro Ser Pro His Val Asp Trp Ser
5425 5430 5435 5440

gcg ggg gcg gtg cag ctg ctg acg gag acg gtg ccc tgg ccc ggc ggg 16422
Ala Gly Ala Val Gln Leu Leu Thr Glu Thr Val Pro Trp Pro Gly Gly
5445 5450 5455

gag ggg cgg ctg cgg cgg gca gga gtg tca tcg ttc ggc gtc agc ggc 16470
Glu Gly Arg Leu Arg Arg Ala Gly Val Ser Ser Phe Gly Val Ser Gly
5460 5465 5470

acc aac gcc cac gtc atc ctc gaa gaa gca ccc gcc cac aac atc ccg 16518

Thr Asn Ala His Val Ile Leu Glu Glu Ala Pro Ala His Asn Ile Pro
5475 5480 5485

tca gac aca ccc gcc gac gac gcc ccg gga gaa gca gcc gcc gac gat 16566
Ser Asp Thr Pro Ala Asp Asp Ala Pro Gly Glu Ala Ala Ala Asp Asp
5490 5495 5500

gtt ccg ggg gaa gcg gcc ggc gac gac gcc ggt acc ggc ggg gaa gcg 16614
Val Pro Gly Glu Ala Ala Gly Asp Asp Ala Gly Thr Gly Gly Glu Ala
5505 5510 5515 5520

act ggt cct gct gcc ggc agt cca ggg gtg tgg ccg tgg ctg gtg tcg 16662
Thr Gly Pro Ala Ala Gly Ser Pro Gly Val Trp Pro Trp Leu Val Ser
5525 5530 5535

gcc aag tcg cag ccg gcc ctg cgc gcc cag gcc cag gcc ctg cac gcc 16710
Ala Lys Ser Gln Pro Ala Leu Arg Ala Gln Ala Gln Ala Leu His Ala
5540 5545 5550

cac ctc acc gac cac ccc ggc ctc gac ctc gcc gac gtc ggg tac acc 16758
His Leu Thr Asp His Pro Gly Leu Asp Leu Ala Asp Val Gly Tyr Thr
5555 5560 5565

ctc gcc cac gcc cgc gcc gtg ttc gac cac cgc gcc acc ctc atc gcc 16806
Leu Ala His Ala Arg Ala Val Phe Asp His Arg Ala Thr Leu Ile Ala
5570 5575 5580

gcc gac cgc gac acc ttc ctg caa gca ctc cag gca ctc gcc gca ggc 16854
Ala Asp Arg Asp Thr Phe Leu Gln Ala Leu Gln Ala Leu Ala Ala Gly
5585 5590 5595 5600

gaa ccc cac ccc gcc gtc atc cac agc agc gcc cca ggc ggg acc ggg 16902
Glu Pro His Pro Ala Val Ile His Ser Ser Ala Pro Gly Gly Thr Gly
5605 5610 5615

acc ggg gag gcc gca gga aag acc gca ttc atc tgc tcc gga cag ggc 16950
Thr Gly Glu Ala Ala Gly Lys Thr Ala Phe Ile Cys Ser Gly Gln Gly
5620 5625 5630

acc caa cgc ccc ggc atg gcc cac ggc ctc tac cac acc cac ccc gtc 16998
Thr Gln Arg Pro Gly Met Ala His Gly Leu Tyr His Thr His Pro Val
5635 5640 5645

ttc gcc gcc gca ctc aac gac atc tgc acc cac ctc gac ccc cac ctc 17046
Phe Ala Ala Ala Leu Asn Asp Ile Cys Thr His Leu Asp Pro His Leu
5650 5655 5660

gac cac ccc ctc ctc ccc ctc ctc acc cag gac ccc aac acc cag gac 17094
Asp His Pro Leu Leu Pro Leu Leu Thr Gln Asp Pro Asn Thr Gln Asp
5665 5670 5675 5680

acc acc acc ctc gaa gaa gcg gcc gca ctg ctc cag cag acc ccg tac 17142
Thr Thr Thr Leu Glu Glu Ala Ala Ala Leu Leu Gln Gln Thr Pro Tyr
5685 5690 5695

gcc cag ccc gcc ctc ttc gcc ttc cag gtc gcc ctc cac cgc ctc ctc 17190
Ala Gln Pro Ala Leu Phe Ala Phe Gln Val Ala Leu His Arg Leu Leu
5700 5705 5710

acc gac ggc tac cac atc acc ccc cac tac tac gcc gga cac tcc ctc 17238
Thr Asp Gly Tyr His Ile Thr Pro His Tyr Tyr Ala Gly His Ser Leu
5715 5720 5725

ggc gaa atc acc gcc gcc cac ctc gcc ggc atc ctc acc ctc acc gac 17286
Gly Glu Ile Thr Ala Ala His Leu Ala Gly Ile Leu Thr Leu Thr Asp
5730 5735 5740

gcc acc acc ctc atc acc caa cgc gcc acc ctc atg caa acc atg ccc 17334
Ala Thr Thr Leu Ile Thr Gln Arg Ala Thr Leu Met Gln Thr Met Pro
5745 5750 5755 5760

ccc ggc acc atg acc acc ctc cac acc acc ccc cac cac atc acc cac 17382
Pro Gly Thr Met Thr Thr Leu His Thr Thr Pro His His Ile Thr His
5765 5770 5775

cac ctc acc gcc cac gaa aac gac ctc gcc atc gcc gcc atc aac acc 17430

His Leu Thr Ala His Glu Asn Asp Leu Ala Ile Ala Ala Ile Asn Thr
5780 5785 5790

ccc acc tcc ctc gtc atc agc ggc acc ccc cac acc gtc caa cac atc 17478
Pro Thr Ser Leu Val Ile Ser Gly Thr Pro His Thr Val Gln His Ile
5795 5800 5805

acc acc ctc tgc caa caa caa ggc atc aaa acc aaa acc ctc ccc acc 17526
Thr Thr Leu Cys Gln Gln Gln Gly Ile Lys Thr Lys Thr Leu Pro Thr
5810 5815 5820

aaa aac gcc ttc cac tcc ccc cac acc aac ccc atc ctc aac caa ctc 17574
Lys Asn Ala Phe His Ser Pro His Thr Asn Pro Ile Leu Asn Gln Leu
5825 5830 5835 5840

cac cag cac acc caa acc ctc acc tac cac cca ccc cac acc ccc ctc 17622
His Gln His Thr Gln Thr Leu Thr Tyr His Pro Pro His Thr Pro Leu
5845 5850 5855

atc acc gcc aac acc cca ccc gac caa ctc ctc acc ccc cac tac tgg 17670
Ile Thr Ala Asn Thr Pro Pro Asp Gln Leu Leu Thr Pro His Tyr Trp
5860 5865 5870

acc caa caa gcc cgc aac acc gtc gac tac gcc acc acc acc caa acc 17718
Thr Gln Gln Ala Arg Asn Thr Val Asp Tyr Ala Thr Thr Thr Gln Thr
5875 5880 5885

ctc cac caa cac ggc gtc acc acc tac atc gaa ctc gga ccc gac aac 17766
Leu His Gln His Gly Val Thr Thr Tyr Ile Glu Leu Gly Pro Asp Asn
5890 5895 5900

acc ctc acc acc ctc acc cac cac aac ctc ccc aac acc ccc acc acc 17814
Thr Leu Thr Thr Leu Thr His His Asn Leu Pro Asn Thr Pro Thr Thr
5905 5910 5915 5920

acc ctc acc ctc acc cac ccc cac cac cac ccc caa acc cac ctc ctc 17862
Thr Leu Thr Leu Thr His Pro His His His Pro Gln Thr His Leu Leu
5925 5930 5935

acc aac ctc gcc aaa acc acc acc acc tgg cac ccc cac cac tac acc 17910
Thr Asn Leu Ala Lys Thr Thr Thr Thr Trp His Pro His His Tyr Thr
5940 5945 5950

cac cac cac aac caa ccc cac acc cac acc cac ctc gac ctc ccc acc 17958
His His His Asn Gln Pro His Thr His Thr His Leu Asp Leu Pro Thr
5955 5960 5965

tac ccc ttc caa cac cag cac tac tgg ctc gaa agc aca cag ccg ggt 18006
Tyr Pro Phe Gln His Gln His Tyr Trp Leu Glu Ser Thr Gln Pro Gly
5970 5975 5980

gcc gga tcc ggt tcg ggt tcc ggt tcc ggg cgg gca ggg act gcg ggc 18054
Ala Gly Ser Gly Ser Gly Ser Gly Ser Gly Arg Ala Gly Thr Ala Gly
5985 5990 5995 6000

ggg acg gca gag gtg gag tcg cgg ttc tgg gac gcg gtg gcc cgc cag 18102
Gly Thr Ala Glu Val Glu Ser Arg Phe Trp Asp Ala Val Ala Arg Gln
6005 6010 6015

gac ctg gaa acg gtc gcg acc acg ctc gcc gtg ccc ccc tcc gcc ggc 18150
Asp Leu Glu Thr Val Ala Thr Thr Leu Ala Val Pro Pro Ser Ala Gly
6020 6025 6030

ctg gac acg gtg gtg ccc gca ctc tcc gcc tgg cac cgc cac caa cac 18198
Leu Asp Thr Val Val Pro Ala Leu Ser Ala Trp His Arg His Gln His
6035 6040 6045

gac caa gcc cgc atc aac acc tgg acc tac cag gaa acc tgg aaa ccc 18246
Asp Gln Ala Arg Ile Asn Thr Trp Thr Tyr Gln Glu Thr Trp Lys Pro
6050 6055 6060

ctc acc ctc ccc acc acc cac caa ccc cac caa acc tgg ctc atc gcc 18294
Leu Thr Leu Pro Thr Thr His Gln Pro His Gln Thr Trp Leu Ile Ala
6065 6070 6075 6080

atc ccc gaa acc cag acc cac cac ccc cac atc acc aac atc ctc acc 18342

Ile Pro Glu Thr Gln Thr His His Pro His Ile Thr Asn Ile Leu Thr
6085 6090 6095

aac ctc cac cac cac ggc atc acc ccc atc ccc ctc acc ctc aac cac 18390
Asn Leu His His His Gly Ile Thr Pro Ile Pro Leu Thr Leu Asn His
6100 6105 6110

acc cac acc aac ccc caa cac ctc cac cac acc cga caa caa gcc caa 18438
Thr His Thr Asn Pro Gln His Leu His His Thr Arg Gln Gln Ala Gln
6115 6120 6125

aac cac acc acc gga ccc atc acc ggc ctg ctc tcc ctc ctc gcc ctc 18486
Asn His Thr Thr Gly Pro Ile Thr Gly Leu Leu Ser Leu Leu Ala Leu
6130 6135 6140

gac gaa aca ccc cac ccc cac cac ccc cac aca ccc acc ggc acc ctc 18534
Asp Glu Thr Pro His Pro His His Pro His Thr Pro Thr Gly Thr Leu
6145 6150 6155 6160

ctc aac ctc acc ctc acc caa acc cac acc caa acc cac cca cca acc 18582
Leu Asn Leu Thr Leu Thr Gln Thr His Thr Gln Thr His Pro Pro Thr
6165 6170 6175

ccc ctc tgg tac gcc acc acc aac gcc acc acc acc cac ccc aac gac 18630
Pro Leu Trp Tyr Ala Thr Thr Asn Ala Thr Thr Thr His Pro Asn Asp
6180 6185 6190

ccc ctc aca cac ccc acc caa gcc caa acc tgg gga ctc gcc cgc acc 18678
Pro Leu Thr His Pro Thr Gln Ala Gln Thr Trp Gly Leu Ala Arg Thr
6195 6200 6205

acc ctc ctc gaa cac ccc acc cac acc gcc gga atc atc gac ctc ccc 18726
Thr Leu Leu Glu His Pro Thr His Thr Ala Gly Ile Ile Asp Leu Pro
6210 6215 6220

acc acc ccc acc ccc cac acc ctc cac cac ctc acc caa acc ctc acc 18774
Thr Thr Pro Thr Pro His Thr Leu His His Leu Thr Gln Thr Leu Thr
6225 6230 6235 6240

caa ccc cac cac caa acc caa ctc gcc atc cgc acc acc ggc acc cac 18822
Gln Pro His His Gln Thr Gln Leu Ala Ile Arg Thr Thr Gly Thr His
6245 6250 6255

acc cgc cgc ctc acc ccc acc acc ctc acc ccc aca cac caa cca ccc 18870
Thr Arg Arg Leu Thr Pro Thr Thr Leu Thr Pro Thr His Gln Pro Pro
6260 6265 6270

acc ccc acc ccc cac gga acc acc ctc atc acc ggc gga acc ggc gcc 18918
Thr Pro Thr Pro His Gly Thr Thr Leu Ile Thr Gly Gly Thr Gly Ala
6275 6280 6285

ctc gcc acc cac ctc acc cac cac ctc acc acc cac caa ccc acc caa 18966
Leu Ala Thr His Leu Thr His His Leu Thr Thr His Gln Pro Thr Gln
6290 6295 6300

cac ctc ctc ctc acc agc cga acc ggc ccc cac acc ccc cac gca caa 19014
His Leu Leu Leu Thr Ser Arg Thr Gly Pro His Thr Pro His Ala Gln
6305 6310 6315 6320

cac ctc acc acc caa ctc caa caa aaa ggc atc cac ctc acc atc acc 19062
His Leu Thr Thr Gln Leu Gln Gln Lys Gly Ile His Leu Thr Ile Thr
6325 6330 6335

acc tgc gac acc agc aac cca gac caa ctc caa caa ctc ctc aac acc 19110
Thr Cys Asp Thr Ser Asn Pro Asp Gln Leu Gln Gln Leu Leu Asn Thr
6340 6345 6350

atc ccc cca caa cac ccc ctc acc acc gtc atc cac acc gca ggc atc 19158
Ile Pro Pro Gln His Pro Leu Thr Thr Val Ile His Thr Ala Gly Ile
6355 6360 6365

ctc gac gac gcc acc ctc acc aac ctc acc ccc acc caa ctc aac aac 19206
Leu Asp Asp Ala Thr Leu Thr Asn Leu Thr Pro Thr Gln Leu Asn Asn
6370 6375 6380

gtc ctc cgc gcc aaa gcc cac agc gcc cac ctc ctc cac caa ctc acc 19254

Val Leu Arg Ala Lys Ala His Ser Ala His Leu Leu His Gln Leu Thr
6385 6390 6395 6400

caa cac acc ccc ctc aac gcc ttc gtc ctc tac tcc tcc gcc gcc gcc 19302
Gln His Thr Pro Leu Asn Ala Phe Val Leu Tyr Ser Ser Ala Ala Ala
6405 6410 6415

acc ttc ggc gca ccc ggc caa gcc aac tac gcc gca gcc aac gcc tac 19350
Thr Phe Gly Ala Pro Gly Gln Ala Asn Tyr Ala Ala Ala Asn Ala Tyr
6420 6425 6430

ctc gac gcc ctc gcc cac cac cgc cac acc cac cac ctc ccc gcc acc 19398
Leu Asp Ala Leu Ala His His Arg His Thr His His Leu Pro Ala Thr
6435 6440 6445

agc atc gcc tgg ggc acc tgg caa gga aac gga ctg gcg act ggt caa 19446
Ser Ile Ala Trp Gly Thr Trp Gln Gly Asn Gly Leu Ala Thr Gly Gln
6450 6455 6460

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Val Ser Glu His Leu Arg Arg Arg Gly Met Phe Ala Met Pro Pro Glu
6465 6470 6475 6480

ttg gcg gtc aca gct gtt gac ggc gcg atc gcg agc ggg cgc ccg agt 19542
Leu Ala Val Thr Ala Val Asp Gly Ala Ile Ala Ser Gly Arg Pro Ser
6485 6490 6495

ctc ctc gtc gcc gat atc gac tgg aag aaa ttg gga ccg gtt ctc tcc 19590
Leu Leu Val Ala Asp Ile Asp Trp Lys Lys Leu Gly Pro Val Leu Ser
6500 6505 6510

agc aag tcg tcg gtc ttg ctc gag gac ctt ccc cag gca cag gga act 19638
Ser Lys Ser Ser Val Leu Leu Glu Asp Leu Pro Gln Ala Gln Gly Thr
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gag gag gcg cgc agt acc gtt gag cag acg gag agc aca aac ctc cgg 19686
Glu Glu Ala Arg Ser Thr Val Glu Gln Thr Glu Ser Thr Asn Leu Arg
6530 6535 6540

caa ctc ctc atg ggt cgg tca cgt tcc gag cag gaa gaa gag ctg ctc 19734
Gln Leu Leu Met Gly Arg Ser Arg Ser Glu Gln Glu Glu Leu Leu
6545 6550 6555 6560

agc ctc gtc cgc atc cac tcc gcg gca gtg ctc ggg cgc gac gac tcc 19782
Ser Leu Val Arg Ile His Ser Ala Ala Val Leu Gly Arg Asp Asp Ser
6565 6570 6575

gag gcc atc ccg ccc ggt cgg ctg ttc agg gat cta ggg ttc gac tcg 19830
Glu Ala Ile Pro Pro Gly Arg Leu Phe Arg Asp Leu Gly Phe Asp Ser
6580 6585 6590

ctt gcg gcg gtg gag ctt cgc aac cac ctc gca gca cag acg gag ctg 19878
Leu Ala Ala Val Glu Leu Arg Asn His Leu Ala Ala Gln Thr Glu Leu
6595 6600 6605

gct ctg ccg acg act ctc gtc ttc gat tac ccc agc ccc acc aag ctc 19926
Ala Leu Pro Thr Thr Leu Val Phe Asp Tyr Pro Ser Pro Thr Lys Leu
6610 6615 6620

gcc caa ttt ctg ctc tcc gag atc gcg gag ttc cag ccc gac aac tca 19974
Ala Gln Phe Leu Leu Ser Glu Ile Ala Glu Phe Gln Pro Asp Asn Ser
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act ccg ctt ccg cga ccc cgg gca gag ctc gat gag ccg atc gcc atc 20022
Thr Pro Leu Pro Arg Pro Arg Ala Glu Leu Asp Glu Pro Ile Ala Ile
6645 6650 6655

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Val Gly Met Ala Cys Arg Phe Pro Gly Gly Val Thr Ser Ala Asp Asp
6660 6665 6670

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Phe Trp Asp Leu Ile Ser Ser Glu Gln Asp Ala Ile Gly Gly Phe Pro
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Thr Asp Arg Gly Trp Asp Leu Asp Thr Leu Tyr Asp Pro Asp Pro Asp
6690 6695 6700

cac ccc ggc acc tgc tac acc cga aac ggc gga ttc ctc tac gac gca 20214
His Pro Gly Thr Cys Tyr Thr Arg Asn Gly Gly Phe Leu Tyr Asp Ala
6705 6710 6715 6720

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Gly His Phe Asp Ala Glu Phe Phe Gly Ile Ser Pro Arg Glu Ala Leu
6725 6730 6735

gcc atg gac ccc cag caa cga ctc ctc ctc gaa acc gcc tgg gaa acc 20310
Ala Met Asp Pro Gln Gln Arg Leu Leu Leu Glu Thr Ala Trp Glu Thr
6740 6745 6750

atc gaa cac gcc ggc atc aac ccc cac acc ctc cac ggc acc ccc acc 20358
Ile Glu His Ala Gly Ile Asn Pro His Thr Leu His Gly Thr Pro Thr
6755 6760 6765

gga gtc ttc acc ggc acc aac gga cag gac cac gcg gca cac atc cgt 20406
Gly Val Phe Thr Gly Thr Asn Gly Gln Asp His Ala Ala His Ile Arg
6770 6775 6780

cag gcc ccg agc ggt acc gag gga ttc gtc ctg acc ggg gca gcc acc 20454
Gln Ala Pro Ser Gly Thr Glu Gly Phe Val Leu Thr Gly Ala Ala Thr
6785 6790 6795 6800

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Ser Ile Ala Ser Gly Arg Ile Ser Tyr Ile Leu Gly Leu Glu Gly Pro
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gcg gtc acc ctc gac aca gcg tgt tcc tcc tcg ctc gtc gcc ctg cac 20550
Ala Val Thr Leu Asp Thr Ala Cys Ser Ser Ser Leu Val Ala Leu His
6820 6825 6830

ctc gcc tgc cag tcc ctc agg tcc ggt gaa tgc acc atg gcc ttg gcc 20598
Leu Ala Cys Gln Ser Leu Arg Ser Gly Glu Cys Thr Met Ala Leu Ala
6835 6840 6845

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Gly Gly Ala Thr Val Met Thr Thr Pro Ile Thr Phe Thr Glu Phe Ala
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cgc caa cgc gga ctc gcc ccc gac ggg cgt tgc aag gcg ttc tcg gcg 20694
Arg Gln Arg Gly Leu Ala Pro Asp Gly Arg Cys Lys Ala Phe Ser Ala
6865 6870 6875 6880

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Ala Ala Asp Gly Thr Gly Trp Gly Glu Gly Val Gly Met Leu Leu Val
6885 6890 6895

gag cgg ctc tcc gac gcc cgc cgc aac ggt cac cgt gtc ctg gcc gtg 20790
Glu Arg Leu Ser Asp Ala Arg Arg Asn Gly His Arg Val Leu Ala Val
6900 6905 6910

gtg cgt ggc agt gcg gtc aac cag gac ggt gcg agc aac ggt ctg acc 20838
Val Arg Gly Ser Ala Val Asn Gln Asp Gly Ala Ser Asn Gly Leu Thr
6915 6920 6925

gcg ccc aac ggg ccc tcc cag cag cgc gtc atc cgc cag gcc ctc gcc 20886
Ala Pro Asn Gly Pro Ser Gln Gln Arg Val Ile Arg Gln Ala Leu Ala
6930 6935 6940

aac gcg gac ctg acc ccc gcc gac gtc gat gcg gtg gag gcc cac ggc 20934
Asn Ala Asp Leu Thr Pro Ala Asp Val Asp Ala Val Glu Ala His Gly
6945 6950 6955 6960

acc ggc acc act ttg ggc gac ccg atc gag gcc cag gcc atc ctc gcg 20982
Thr Gly Thr Thr Leu Gly Asp Pro Ile Glu Ala Gln Ala Ile Leu Ala
6965 6970 6975

acc tac gga cag gac cgt ccc ggc aac ggg ccg ttg tgg ctg ggc tcc 21030
Thr Tyr Gly Gln Asp Arg Pro Gly Asn Gly Pro Leu Trp Leu Gly Ser
6980 6985 6990

gtc aag tcc aac gtc gga cac aca cag gcc gcg gcg ggc gtg gcc gga 21078

Val Lys Ser Asn Val Gly His Thr Gln Ala Ala Ala Gly Val Ala Gly
6995 7000 7005

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Val Ile Lys Met Val Met Ala Leu Arg His Arg Thr Leu Pro Pro Thr
7010 7015 7020

ctc cac gcg gat gag ccg tcg ccg cat gtg gac tgg tcc gcg ggt gcg 21174
Leu His Ala Asp Glu Pro Ser Pro His Val Asp Trp Ser Ala Gly Ala
7025 7030 7035 7040

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Val Gln Leu Leu Thr Glu Thr Val Pro Trp Pro Gly Gly Glu Gly Arg
7045 7050 7055

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Pro Arg Arg Ala Gly Val Ser Ser Phe Gly Val Ser Gly Thr Asn Ala
7060 7065 7070

cac gtc atc ctc gaa gaa gca ccc gcc gac gac gtt ccg ggg gga cca 21318
His Val Ile Leu Glu Glu Ala Pro Ala Asp Asp Val Pro Gly Gly Pro
7075 7080 7085

ccc gcc gac gag gat gcc ggt agt ggc gag gag gct gct gcc ggc agt 21366
Pro Ala Asp Glu Asp Ala Gly Ser Gly Glu Glu Ala Ala Ala Gly Ser
7090 7095 7100

cct ggg gtg tgg ccg tgg ctg gtg tcg gcc aag tcg cag ccg gcc ctg 21414
Pro Gly Val Trp Pro Trp Leu Val Ser Ala Lys Ser Gln Pro Ala Leu
7105 7110 7115 7120

cgc gcc cag gcc cag gcc ctg cac gcc cac ctc acc gac cac ccc ggc 21462
Arg Ala Gln Ala Gln Ala Leu His Ala His Leu Thr Asp His Pro Gly
7125 7130 7135

ctc gac ctc gcc gac gtc gga tac acc ctc gcc cac gcc cgc gcc gtg 21510
Leu Asp Leu Ala Asp Val Gly Tyr Thr Leu Ala His Ala Arg Ala Val
7140 7145 7150

ttc gac cac cgc gcc acc ctc atc gcc gcc gac cgc gac acc ttc ctg 21558
Phe Asp His Arg Ala Thr Leu Ile Ala Ala Asp Arg Asp Thr Phe Leu
7155 7160 7165

caa gca ctc cag gca ctc gcc gca ggc gaa ccc cac ccc gcc gtc atc 21606
Gln Ala Leu Gln Ala Leu Ala Ala Gly Glu Pro His Pro Ala Val Ile
7170 7175 7180

cac agc agc gcc cca ggc ggg acc ggg acc ggg gag gcc gca gga aag 21654
His Ser Ser Ala Pro Gly Gly Thr Gly Thr Gly Glu Ala Ala Gly Lys
7185 7190 7195 7200

acc gca ttc atc tgc tcc gga cag ggc acc caa cgc ccc ggc atg gcc 21702
Thr Ala Phe Ile Cys Ser Gly Gln Gly Thr Gln Arg Pro Gly Met Ala
7205 7210 7215

cac ggc ctc tac cac acc cac ccc gtc ttc gcc gcc gca ctc aac gac 21750
His Gly Leu Tyr His Thr His Pro Val Phe Ala Ala Ala Leu Asn Asp
7220 7225 7230

atc tgc acc cac ctc gac ccc cac ctc gac cac ccc ctc ctc ccc ctc 21798
Ile Cys Thr His Leu Asp Pro His Leu Asp His Pro Leu Leu Pro Leu
7235 7240 7245

ctc acc caa aac gac aac gac aac gac aac gag gac gcg gcc gca ctg 21846
Leu Thr Gln Asn Asp Asn Asp Asn Asp Asn Glu Asp Ala Ala Ala Leu
7250 7255 7260

ctc cag cag acc ccg tac gcc cag ccc gcc ctc ttc gcc ttc cag gtc 21894
Leu Gln Gln Thr Pro Tyr Ala Gln Pro Ala Leu Phe Ala Phe Gln Val
7265 7270 7275 7280

gcc ctc cac cgc ctc ctc acc gac ggc tac cac atc acc ccc cac tac 21942
Ala Leu His Arg Leu Leu Thr Asp Gly Tyr His Ile Thr Pro His Tyr
7285 7290 7295

tac gcc gga cac tcc ctc ggc gaa atc acc gcc gcc cac ctc gcc ggc 21990

Tyr Ala Gly His Ser Leu Gly Glu Ile Thr Ala Ala His Leu Ala Gly
7300 7305 7310

atc ctc acc ctc acc gac gcc acc acc ctc atc acc caa cgc gcc acc 22038
Ile Leu Thr Leu Thr Asp Ala Thr Thr Leu Ile Thr Gln Arg Ala Thr
7315 7320 7325

ctc atg caa acc atg ccc ccc ggc acc atg acc acc ctc cac acc acc 22086
Leu Met Gln Thr Met Pro Pro Gly Thr Met Thr Thr Leu His Thr Thr
7330 7335 7340

cca cac cac atc acc cac cac ctc acc gcc cac gaa aac gac ctc gcc 22134
Pro His His Ile Thr His His Leu Thr Ala His Glu Asn Asp Leu Ala
7345 7350 7355 7360

atc gcc gcc atc aac acc ccc acc tcc ctc gtc atc agc ggc acc ccc 22182
Ile Ala Ala Ile Asn Thr Pro Thr Ser Leu Val Ile Ser Gly Thr Pro
7365 7370 7375

cac acc gtc caa cac atc acc acc ctc tgc caa caa caa ggc atc aaa 22230
His Thr Val Gln His Ile Thr Thr Leu Cys Gln Gln Gln Gly Ile Lys
7380 7385 7390

acc aaa acc ctc ccc acc aac cac gcc ttc cac tcc ccc cac acc aac 22278
Thr Lys Thr Leu Pro Thr Asn His Ala Phe His Ser Pro His Thr Asn
7395 7400 7405

ccc atc ctc aac caa ctc cac cag cac acc caa acc ctc acc tac cac 22326
Pro Ile Leu Asn Gln Leu His Gln His Thr Gln Thr Leu Thr Tyr His
7410 7415 7420

cca ccc cac acc ccc ctc atc acc gcc aac acc cca ccc gac caa ctc 22374
Pro Pro His Thr Pro Leu Ile Thr Ala Asn Thr Pro Pro Asp Gln Leu
7425 7430 7435 7440

ctc acc ccc cac tac tgg acc caa caa gcc cgc aac acc gtc gac tac 22422
Leu Thr Pro His Tyr Trp Thr Gln Gln Ala Arg Asn Thr Val Asp Tyr
7445 7450 7455

gcc acc acc acc caa acc ctc cac caa cac ggc gtc acc acc tac atc 22470
Ala Thr Thr Thr Gln Thr Leu His Gln His Gly Val Thr Thr Tyr Ile
7460 7465 7470

gaa ctc gga ccc gac aac acc ctc acc acc ctc acc cac cac aac ctc 22518
Glu Leu Gly Pro Asp Asn Thr Leu Thr Thr Leu Thr His His Asn Leu
7475 7480 7485

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Pro Asn Thr Pro Thr Thr Thr Leu Thr Leu Thr His Pro His His His
7490 7495 7500

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Pro Gln Thr His Leu Leu Thr Asn Leu Ala Lys Thr Thr Thr Thr Trp
7505 7510 7515 7520

cac ccc cac cac tac acc cac cac cac aac caa ccc cac acc cac acc 22662
His Pro His His Tyr Thr His His His Asn Gln Pro His Thr His Thr
7525 7530 7535

cac ctc gac ctc ccc acc tac ccc ttc caa cac cac cac tac tgg ctc 22710
His Leu Asp Leu Pro Thr Tyr Pro Phe Gln His His His Tyr Trp Leu
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Glu Leu Pro Ser Ala Gln Thr Ser Pro Gly Gln Arg Arg Ser Arg Arg
7555 7560 7565

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Ser Ala Pro Asp Thr Ala Glu Ser Glu Phe Trp Asp Ala Val Asn Glu
7570 7575 7580

gaa gac ctc cag agc ctc gcc gaa acc ctc gac atc gac gcc tct gct 22854
Glu Asp Leu Gln Ser Leu Ala Glu Thr Leu Asp Ile Asp Ala Ser Ala
7585 7590 7595 7600

ctg gac acg gtg gtg ccc gca ctc tcc gcc tgg cac cgc cac caa cac 22902

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Leu Asp Thr Val Val Pro Ala Leu Ser Ala Trp His Arg His Gln His
7605 7610 7615

gac caa gcc cgc atc aac acc tgg acc tac cag gaa acc tgg aaa ccc 22950
Asp Gln Ala Arg Ile Asn Thr Trp Thr Tyr Gln Glu Thr Trp Lys Pro
7620 7625 7630

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Leu Thr Leu Pro Thr Thr His Gln Pro His Gln Thr Trp Leu Ile Ala
7635 7640 7645

atc ccc gaa acc cag acc cac cac ccc cac atc acc aac atc ctc acc 23046
Ile Pro Glu Thr Gln Thr His His Pro His Ile Thr Asn Ile Leu Thr
7650 7655 7660

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Asn Leu His His His Gly Ile Thr Pro Ile Pro Leu Thr Val Asn His
7665 7670 7675 7680

acc cac acc aac ccc caa cac ctc cac cac acc ctc cac cac acc cga 23142
Thr His Thr Asn Pro Gln His Leu His His Thr Leu His His Thr Arg
7685 7690 7695

caa caa gcc caa aac cac acc acc gga ccc atc acc ggc ctg ctc tcc 23190
Gln Gln Ala Gln Asn His Thr Thr Gly Pro Ile Thr Gly Leu Leu Ser
7700 7705 7710

ctc ctc gcc ctc gac gaa aca ccc cac ccc cac cac ccc cac aca ccc 23238
Leu Leu Ala Leu Asp Glu Thr Pro His Pro His His Pro His Thr Pro
7715 7720 7725

acc ggc acc ctc ctc aac ctc acc ctc ccc caa acc cac acc caa acc 23286
Thr Gly Thr Leu Leu Asn Leu Thr Leu Pro Gln Thr His Thr Gln Thr
7730 7735 7740

cac cca cca acc ccc ctc tgg tac gcc acc acc aac gcc acc acc acc 23334
His Pro Pro Thr Pro Leu Trp Tyr Ala Thr Thr Asn Ala Thr Thr Thr
7745 7750 7755 7760

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cac ccc aac gac ccc ctc aca cac ccc acc caa gcc caa acc tgg gga 23382
His Pro Asn Asp Pro Leu Thr His Pro Thr Gln Ala Gln Thr Trp Gly
7765 7770 7775

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Leu Ala Arg Thr Thr Leu Leu Glu His Pro Thr His Thr Ala Gly Ile
7780 7785 7790

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Ile Asp Leu Pro Thr Thr Pro Thr Pro His Thr Leu His His Leu Thr
7795 7800 7805

caa acc ctc acc caa ccc cac cac caa acc caa ctc gcc atc cgc acc 23526
Gln Thr Leu Thr Gln Pro His His Gln Thr Gln Leu Ala Ile Arg Thr
7810 7815 7820

acc ggc acc cac acc cgc cgc ctc acc ccc acc acc ctc acc ccc aca 23574
Thr Gly Thr His Thr Arg Arg Leu Thr Pro Thr Thr Leu Thr Pro Thr
7825 7830 7835 7840

cac caa cca ccc acc ccc acc ccc cac gga acc acc ctc atc acc ggc 23622
His Gln Pro Pro Thr Pro Thr Pro His Gly Thr Thr Leu Ile Thr Gly
7845 7850 7855

gga acc ggc gcc ctc gcc acc cac ctc acc cac cac ctc acc acc cac 23670
Gly Thr Gly Ala Leu Ala Thr His Leu Thr His His Leu Thr Thr His
7860 7865 7870

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Gln Pro Thr Gln His Leu Leu Leu Thr Ser Arg Thr Gly Pro His Thr
7875 7880 7885

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Pro His Ala Gln His Leu Thr Thr Gln Leu Gln Gln Lys Gly Ile His
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Thr Ala Gly Val Asn Leu Phe Ala Pro Val Ser Glu Thr Asp Ala Glu
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Ser Phe Ser Ser Val Thr Ala Ala Lys Ala Thr Gly Ala Ala Ile Leu
7955 7960 7965

cat gag ttg ctg ctg gac cat gaa acg ctt gaa cac ttc att ctc ttc 24006
His Glu Leu Leu Leu Asp His Glu Thr Leu Glu His Phe Ile Leu Phe
7970 7975 7980

tcg tcg ggc gcc ggc gct tgg ggc agc ggg aat cag tgc gca tac tcg 24054
Ser Ser Gly Ala Gly Ala Trp Gly Ser Gly Asn Gln Cys Ala Tyr Ser
7985 7990 7995 8000

gcg gcc aac gca tac ctg gac gcg ctc gcg acg cat cgt cag aca cat 24102
Ala Ala Asn Ala Tyr Leu Asp Ala Leu Ala Thr His Arg Gln Thr His
8005 8010 8015

gga ctt ccc ggg gca tcg atc gcc tgg ggc ccc tgg gcc gga aag ggc 24150
Gly Leu Pro Gly Ala Ser Ile Ala Trp Gly Pro Trp Ala Gly Lys Gly
8020 8025 8030

atg tcg gcc ggt gat gcg gct cat ggt tac ctg gaa aag cgc ggc att 24198
Met Ser Ala Gly Asp Ala Ala His Gly Tyr Leu Glu Lys Arg Gly Ile
8035 8040 8045

ctg ccg atg gag cca cgc atg gcg ctc gcg gca ttc cat cgt gcg cgg 24246
Leu Pro Met Glu Pro Arg Met Ala Leu Ala Ala Phe His Arg Ala Arg
8050 8055 8060

gcg cag cgg ccg aat tcc aac ctg atc atc gcg gac atc gac tgg gag 24294
Ala Gln Arg Pro Asn Ser Asn Leu Ile Ile Ala Asp Ile Asp Trp Glu
8065 8070 8075 8080

cgc ttc gtc ccc gcc ttc acc gct cga cgc cac agc ccg ctc atc gag 24342
Arg Phe Val Pro Ala Phe Thr Ala Arg Arg His Ser Pro Leu Ile Glu
8085 8090 8095

gac att ccg gag gtt cgg caa gcg gct cag gag ctg gaa gca gct gcg 24390
Asp Ile Pro Glu Val Arg Gln Ala Ala Gln Glu Leu Glu Ala Ala Ala
8100 8105 8110

tcg acg gca aag acg acc aca gct cag ccg att gcg acg tct ctc cgt 24438
Ser Thr Ala Lys Thr Thr Thr Ala Gln Pro Ile Ala Thr Ser Leu Arg
8115 8120 8125

gag cga ttg gcc cga ctg acg tcc tca aag cag aac cag gtg ctg ctc 24486
Glu Arg Leu Ala Arg Leu Thr Ser Ser Lys Gln Asn Gln Val Leu Leu
8130 8135 8140

ggc ctg att cgg aca ggc atc tgc acc gtt ctc ggc ctt cgt aat ccg 24534
Gly Leu Ile Arg Thr Gly Ile Cys Thr Val Leu Gly Leu Arg Asn Pro
8145 8150 8155 8160

gaa ggc atc gag gac caa cga gcc ttc cgc gac ctc ggc ttc gac tcg 24582
Glu Gly Ile Glu Asp Gln Arg Ala Phe Arg Asp Leu Gly Phe Asp Ser
8165 8170 8175

ctg acg tcg gct cag ttc agc aag gaa ctc gcc aag gaa acc gga ctg 24630
Leu Thr Ser Ala Gln Phe Ser Lys Glu Leu Ala Lys Glu Thr Gly Leu
8180 8185 8190

cca ctc ccc ccg tcc ctg gtc ttc gac tat ccc acc ccg cag gaa tgt 24678
Pro Leu Pro Pro Ser Leu Val Phe Asp Tyr Pro Thr Pro Gln Glu Cys
8195 8200 8205

gct gcc cat ctg cgc aca caa ctc gtc gac cta gac gac gaa gag gac 24726

Ala Ala His Leu Arg Thr Gln Leu Val Asp Leu Asp Asp Glu Glu Asp
8210 8215 8220

gcg gca ctg tcg aat gct ctc ccg caa gtg gcc cat cgg cgt acc gtc 24774
Ala Ala Leu Ser Asn Ala Leu Pro Gln Val Ala His Arg Arg Thr Val
8225 8230 8235 8240

gag gac gaa ccg atc gcc atc atc ggt atg gca tgt cgc ttc ccc ggc 24822
Glu Asp Glu Pro Ile Ala Ile Ile Gly Met Ala Cys Arg Phe Pro Gly
8245 8250 8255

ggc gta cgt tct gcc gac gac ctg tgg gaa ttg ctc gct tcg ggt aag 24870
Gly Val Arg Ser Ala Asp Asp Leu Trp Glu Leu Leu Ala Ser Gly Lys
8260 8265 8270

gac gct atc ggc gtc ttc ccg acc gac cgc ggc tgg gac ctg gac acg 24918
Asp Ala Ile Gly Val Phe Pro Thr Asp Arg Gly Trp Asp Leu Asp Thr
8275 8280 8285

ctc tac gac ccc gac ccc gac cac ccc ggc acc tgc tac acc cga aac 24966
Leu Tyr Asp Pro Asp Pro Asp His Pro Gly Thr Cys Tyr Thr Arg Asn
8290 8295 8300

ggc gga ttc ctc tac ggc gca ggc cac ttc gac gcc gaa ttc ttc ggc 25014
Gly Gly Phe Leu Tyr Gly Ala Gly His Phe Asp Ala Glu Phe Phe Gly
8305 8310 8315 8320

atc agc ccc cgc gaa gcc ctc gcc atg gac ccc cag caa cga ctc ctc 25062
Ile Ser Pro Arg Glu Ala Leu Ala Met Asp Pro Gln Gln Arg Leu Leu
8325 8330 8335

ctc gaa acc gcc tgg gaa acc atc gaa cac gcc ggc atc aac ccc cac 25110
Leu Glu Thr Ala Trp Glu Thr Ile Glu His Ala Gly Ile Asn Pro His
8340 8345 8350

acc ctc cac ggc acc ccc acc gga gtc ttc gcc gga atc aac gct caa 25158
Thr Leu His Gly Thr Pro Thr Gly Val Phe Ala Gly Ile Asn Ala Gln
8355 8360 8365

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gac cac gcc gcg cat atc cgc caa agc cgt gat gtg gag acc atc gag 25206
Asp His Ala Ala His Ile Arg Gln Ser Arg Asp Val Glu Thr Ile Glu
8370 8375 8380

ggc tac gcc ctg acc ggc agt tcg gga agt gtg gcg tcc ggc cgg gtg 25254
Gly Tyr Ala Leu Thr Gly Ser Ser Gly Ser Val Ala Ser Gly Arg Val
8385 8390 8395 8400

gcc tac acg ctc ggg ctc gaa ggc ccc gcg gtg tcg gtg gat acg gcg 25302
Ala Tyr Thr Leu Gly Leu Glu Gly Pro Ala Val Ser Val Asp Thr Ala
8405 8410 8415

tgt tcg tcg tcg ttg gtg gcg ttg cat tgg gcg gcg cag gcg ttg cgt 25350
Cys Ser Ser Ser Leu Val Ala Leu His Trp Ala Ala Gln Ala Leu Arg
8420 8425 8430

gcg ggt gag tgt tcg atg gcg ctt gcc ggg ggt gtg acg gtg atg tcg 25398
Ala Gly Glu Cys Ser Met Ala Leu Ala Gly Gly Val Thr Val Met Ser
8435 8440 8445

tct ccg ggt acg ttt gtg gag ttc tca cgt cag cgg ggt ctg gcc gcg 25446
Ser Pro Gly Thr Phe Val Glu Phe Ser Arg Gln Arg Gly Leu Ala Ala
8450 8455 8460

gac ggg cgg tgc aag gcc tat tcg gcg gct gct gac ggt acc ggc tgg 25494
Asp Gly Arg Cys Lys Ala Tyr Ser Ala Ala Ala Asp Gly Thr Gly Trp
8465 8470 8475 8480

gcc gag ggt gtg ggg atg ctg ctg gtg gag cgg ctc tcc gac gcc cgt 25542
Ala Glu Gly Val Gly Met Leu Leu Val Glu Arg Leu Ser Asp Ala Arg
8485 8490 8495

cgc aac ggt cac cgt gtc ctg gcc gtg gtg cgt ggc agt gcg gtc aac 25590
Arg Asn Gly His Arg Val Leu Ala Val Val Arg Gly Ser Ala Val Asn
8500 8505 8510

cag gac ggt gcg agc aac ggt ctg acc gcg ccc aac ggg ccc tcc cag 25638

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Gln Asp Gly Ala Ser Asn Gly Leu Thr Ala Pro Asn Gly Pro Ser Gln
8515 8520 8525

cag cgt gtc atc cgt cag gcc ctg gcc aat gcg gga ctg acc ccg gcc 25686
Gln Arg Val Ile Arg Gln Ala Leu Ala Asn Ala Gly Leu Thr Pro Ala
8530 8535 8540

gat gtc gac gca gtg gag ggc cac ggc acc ggg acc act ctg ggg gac 25734
Asp Val Asp Ala Val Glu Gly His Gly Thr Gly Thr Thr Leu Gly Asp
8545 8550 8555 8560

ccg atc gag gcc cag gca ctc ctg gcc gcc tac gga caa cac cgc ccc 25782
Pro Ile Glu Ala Gln Ala Leu Leu Ala Ala Tyr Gly Gln His Arg Pro
8565 8570 8575

cac cac cgc ccc ttg tgg ctg gga tcc ctc aaa tcc aac atc ggg cac 25830
His His Arg Pro Leu Trp Leu Gly Ser Leu Lys Ser Asn Ile Gly His
8580 8585 8590

gca cag gcc gcc gcg ggc gtg ggc gga gtc atc aag atg gtg atg gcc 25878
Ala Gln Ala Ala Ala Gly Val Gly Gly Val Ile Lys Met Val Met Ala
8595 8600 8605

ctg cgc aac ggg ctg ctg cca cag acc ctc cac gtg gac gag ccc acc 25926
Leu Arg Asn Gly Leu Leu Pro Gln Thr Leu His Val Asp Glu Pro Thr
8610 8615 8620

ccc cag gtc gac tgg tcc aca ggc gca gta caa ctc ctg aca caa ccg 25974
Pro Gln Val Asp Trp Ser Thr Gly Ala Val Gln Leu Leu Thr Gln Pro
8625 8630 8635 8640

gtg ccc tgg ccc gcc gac ccg gcc ggc cgg cca cgc cac gcc ggc gtg 26022
Val Pro Trp Pro Ala Asp Pro Ala Gly Arg Pro Arg His Ala Gly Val
8645 8650 8655

tca tca ttc ggc gtc agc ggc acc aac gcc cac atc atc ctc gaa gaa 26070
Ser Ser Phe Gly Val Ser Gly Thr Asn Ala His Ile Ile Leu Glu Glu
8660 8665 8670

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gca ccc act ccc cag gac agc gat acc gac gac gaa ccg cct gcc aac 26118
Ala Pro Thr Pro Gln Asp Ser Asp Thr Asp Asp Glu Pro Pro Ala Asn
8675 8680 8685

gca cca gcc ctg ccc cat ccc ctc cct ctt ccc gtg ccg gtg tcg gcg 26166
Ala Pro Ala Leu Pro His Pro Leu Pro Leu Pro Val Pro Val Ser Ala
8690 8695 8700

agg tct gag gcc ggg ttg cgg gcg cag gca cag gcg ttg cgc cag tac 26214
Arg Ser Glu Ala Gly Leu Arg Ala Gln Ala Gln Ala Leu Arg Gln Tyr
8705 8710 8715 8720

gtg gca gcc cgc ccg gac atg tca cct gcc gac att ggt gcg ggt ctg 26262
Val Ala Ala Arg Pro Asp Met Ser Pro Ala Asp Ile Gly Ala Gly Leu
8725 8730 8735

gcc cgc ggc cgg gcc gta ctg gaa cac cgc gcc gtc atc ctg gcc gcg 26310
Ala Arg Gly Arg Ala Val Leu Glu His Arg Ala Val Ile Leu Ala Ala
8740 8745 8750

gac cgc gag gaa ctg gcg cag gca ctg aca gcc ctg gca gcc ggc gaa 26358
Asp Arg Glu Glu Leu Ala Gln Ala Leu Thr Ala Leu Ala Ala Gly Glu
8755 8760 8765

ccc cac ccc cac atc acc aca ggc cac acc cgg ggc ggt gac cgc ggc 26406
Pro His Pro His Ile Thr Thr Gly His Thr Arg Gly Gly Asp Arg Gly
8770 8775 8780

ggc gtc gtc ttc gtc ttc ccc gga cag ggc ggc cag tgg gcc ggg atg 26454
Gly Val Val Phe Val Phe Pro Gly Gln Gly Gly Gln Trp Ala Gly Met
8785 8790 8795 8800

ggc ctg acc ctg ctc acc tcc tca ccc gtg ttc gcc gaa cac atc gac 26502
Gly Leu Thr Leu Leu Thr Ser Ser Pro Val Phe Ala Glu His Ile Asp
8805 8810 8815

gca tgc gag aaa gcc ctc acc ccc tgg gtg ccc tgg tcc ctg acc gac 26550

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Replaced by 26694

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Ala Cys Glu Lys Ala Leu Thr Pro Trp Val Pro Trp Ser Leu Thr Asp
          8820                8825                8830

atc ctg cac cgc gac ccc gac gac ccc gca tgg caa caa gcc gac gtg   26598
Ile Leu His Arg Asp Pro Asp Asp Pro Ala Trp Gln Gln Ala Asp Val
       8835                8840                8845

gtc cag ccc gtg ctc ttc agc atc atg gtc tcc ctc gcc gcc ctg tgg   26646
Val Gln Pro Val Leu Phe Ser Ile Met Val Ser Leu Ala Ala Leu Trp
   8850                8855                8860

cgc tcc tac ggc atc gaa ccc gac gcg gtc ctc ggc cac tcc cag gga   26694
Arg Ser Tyr Gly Ile Glu Pro Asp Ala Val Leu Gly His Ser Gln Gly
8865                8870                8875                8880

gaa atc gcc gcc gcc cac atc tgc ggc gca ctc agc ctg aaa gac gcc   26742
Glu Ile Ala Ala Ala His Ile Cys Gly Ala Leu Ser Leu Lys Asp Ala
               8885                8890                8895

gcc aaa acc gtt gca ctg cgc agc cgc gca ctg gcc gcc gta cga ggc   26790
Ala Lys Thr Val Ala Leu Arg Ser Arg Ala Leu Ala Ala Val Arg Gly
          8900                8905                8910

cgg ggc gcc atg gcc tca ctg ccc ctg ccc gcc cag gac gtg cag cag   26838
Arg Gly Ala Met Ala Ser Leu Pro Leu Pro Ala Gln Asp Val Gln Gln
       8915                8920                8925

ctc att tcc gaa cgg tgg gaa ggg cag ttg tgg gtg gca gcc ctc aac   26886
Leu Ile Ser Glu Arg Trp Glu Gly Gln Leu Trp Val Ala Ala Leu Asn
   8930                8935                8940

ggc ccc cac tcc acc acc gtc tcc ggc gac acc aag gcg gtg gat gag   26934
Gly Pro His Ser Thr Thr Val Ser Gly Asp Thr Lys Ala Val Asp Glu
8945                8950                8955                8960

gtg ctg gcg cac tgc acc gac acc ggc cta cgg gcc aaa cgc atc ccc   26982
Val Leu Ala His Cys Thr Asp Thr Gly Leu Arg Ala Lys Arg Ile Pro
               8965                8970                8975
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gtc gac tac gcc tcc cac tgc ccc cac gtc caa ccc ctc cac gac gaa 27030
Val Asp Tyr Ala Ser His Cys Pro His Val Gln Pro Leu His Asp Glu
8980 8985 8990

ctc ctg cac ctg ctg gga gac atc acc ccc cag ccg tcc acc gtg ccg 27078
Leu Leu His Leu Leu Gly Asp Ile Thr Pro Gln Pro Ser Thr Val Pro
8995 9000 9005

ttc ttc tcc acc gtg gaa ggc acc tgg ctg gac acc aca acc ctg gac 27126
Phe Phe Ser Thr Val Glu Gly Thr Trp Leu Asp Thr Thr Thr Leu Asp
9010 9015 9020

gcc gcc tac tgg tac cgc aac ctc cac cag ccc gtc cgc ttc agc cac 27174
Ala Ala Tyr Trp Tyr Arg Asn Leu His Gln Pro Val Arg Phe Ser His
9025 9030 9035 9040

gcc atc cag acc ctg acc gac gac gga cac cgc gcc ttc atc gaa atc 27222
Ala Ile Gln Thr Leu Thr Asp Asp Gly His Arg Ala Phe Ile Glu Ile
9045 9050 9055

agc ccc cac ccc acc ctc gtc ccc gcc atc gaa gac acc acc gaa aac 27270
Ser Pro His Pro Thr Leu Val Pro Ala Ile Glu Asp Thr Thr Glu Asn
9060 9065 9070

acc acc gaa aac atc acc gcg acc ggc agc ctc cgc cgc ggc gac aac 27318
Thr Thr Glu Asn Ile Thr Ala Thr Gly Ser Leu Arg Arg Gly Asp Asn
9075 9080 9085

gac acc cac cgc ttc ctc acc gcc ctc gcc cac acc cac acc acc ggc 27366
Asp Thr His Arg Phe Leu Thr Ala Leu Ala His Thr His Thr Thr Gly
9090 9095 9100

atc ggc aca ccc acc acc tgg cac cac cac tac acc caa acc cac ccc 27414
Ile Gly Thr Pro Thr Thr Trp His His His Tyr Thr Gln Thr His Pro
9105 9110 9115 9120

cac ccc aac ccc cac acc cac ctc gac ctg ccc acc tac ccc ttc caa 27462

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His Pro Asn Pro His Thr His Leu Asp Leu Pro Thr Tyr Pro Phe Gln
9125 9130 9135

cac cag cac tac tgg ctc caa cca ccc acc aca aca acc gac ctc acc 27510
His Gln His Tyr Trp Leu Gln Pro Pro Thr Thr Thr Thr Asp Leu Thr
9140 9145 9150

acc acc ggc ctc acc ccc acc cac cac ccc ctc ctc acc gcc aca ctc 27558
Thr Thr Gly Leu Thr Pro Thr His His Pro Leu Leu Thr Ala Thr Leu
9155 9160 9165

acc ctc gcc gac aac aac aca caa cta ctc acc ggc cgc ctc tcc cta 27606
Thr Leu Ala Asp Asn Asn Thr Gln Leu Leu Thr Gly Arg Leu Ser Leu
9170 9175 9180

cgc acc cac ccc tgg ctc acc gac cac acc gtc gcc ggc atg gtc ctc 27654
Arg Thr His Pro Trp Leu Thr Asp His Thr Val Ala Gly Met Val Leu
9185 9190 9195 9200

ctg ccg ggc acc gcg ctc ctc gaa ctc gcc ctc caa gcc ggc gaa cgg 27702
Leu Pro Gly Thr Ala Leu Leu Glu Leu Ala Leu Gln Ala Gly Glu Arg
9205 9210 9215

gtg gac tgc cct cgg gtg gag gaa ctg acc ctg cac gca ccg ttg gtg 27750
Val Asp Cys Pro Arg Val Glu Glu Leu Thr Leu His Ala Pro Leu Val
9220 9225 9230

atc ccg cac acc gag gac gtg acg ttg cag gtc acc gtt cgg gca gcc 27798
Ile Pro His Thr Glu Asp Val Thr Leu Gln Val Thr Val Arg Ala Ala
9235 9240 9245

gat gag agt ggc cat cgc gcc ctc gcg atc cac tcg tac tcc ggc acc 27846
Asp Glu Ser Gly His Arg Ala Leu Ala Ile His Ser Tyr Ser Gly Thr
9250 9255 9260

gcg tcg tcg gcg gac cgg gag tgg acc cgt cac gcc acg ggc ctc ctc 27894
Ala Ser Ser Ala Asp Arg Glu Trp Thr Arg His Ala Thr Gly Leu Leu
9265 9270 9275 9280

aca cac cac gcc gac acc gat cac cgt gcc gac acg cac acg gac gcg 27942
Thr His His Ala Asp Thr Asp His Arg Ala Asp Thr His Thr Asp Ala
9285 9290 9295

tgc ctt ggc ggg agc tgg ccc ccg ccc ggc gcg cag ccc atc gaa ctg 27990
Cys Leu Gly Gly Ser Trp Pro Pro Pro Gly Ala Gln Pro Ile Glu Leu
9300 9305 9310

ggc gac gtc tac ggt cgt atg gcg gcg gac tcg gac atc gcc tac ggg 28038
Gly Asp Val Tyr Gly Arg Met Ala Ala Asp Ser Asp Ile Ala Tyr Gly
9315 9320 9325

ccg gtc ttc cag ggg ctg cac gcc gcc tgg agg ttc ggc gac gat gtc 28086
Pro Val Phe Gln Gly Leu His Ala Ala Trp Arg Phe Gly Asp Asp Val
9330 9335 9340

ctg gcc gag gtg cgt ctg ccg gaa gag gct ctg cgc gat gct ccg gcg 28134
Leu Ala Glu Val Arg Leu Pro Glu Glu Ala Leu Arg Asp Ala Pro Ala
9345 9350 9355 9360

gcg gcc ttc ggt gtt cac ccg gcc ttg ctc gac gcg gcc ctg cac gcc 28182
Ala Ala Phe Gly Val His Pro Ala Leu Leu Asp Ala Ala Leu His Ala
9365 9370 9375

acg gcg ctc acc ccc cag aac ggg gac ggc tcg acg gag aac gtc gcc 28230
Thr Ala Leu Thr Pro Gln Asn Gly Asp Gly Ser Thr Glu Asn Val Ala
9380 9385 9390

cag gag agc atg cct gac cgc gca gcc cac cag gcg cga ctg ccg ttc 28278
Gln Glu Ser Met Pro Asp Arg Ala Ala His Gln Ala Arg Leu Pro Phe
9395 9400 9405

agc tgg agc ggc gtg tcc ctg cac acg gcg ggc agt tcc gtg ttg cgc 28326
Ser Trp Ser Gly Val Ser Leu His Thr Ala Gly Ser Ser Val Leu Arg
9410 9415 9420

gta cgg ctg tcg cgc agt ccg cag cac ggt aat gcc gtg gcc ctc acc 28374

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Val Arg Leu Ser Arg Ser Pro Gln His Gly Asn Ala Val Ala Leu Thr
9425 9430 9435 9440

gcg gcc gac gag gac ggt cgg ccg gtg gtg acg atc gag tcg ctc gcg 28422
Ala Ala Asp Glu Asp Gly Arg Pro Val Val Thr Ile Glu Ser Leu Ala
9445 9450 9455

ctg cgg ccg gtg tcc acc gag gag ctg cgc gcg gcc gcg gat cgt acg 28470
Leu Arg Pro Val Ser Thr Glu Glu Leu Arg Ala Ala Ala Asp Arg Thr
9460 9465 9470

ccc gag cac gag tcg ctc ttc cga ctg gac tgg gtt tcc gta cca gtg 28518
Pro Glu His Glu Ser Leu Phe Arg Leu Asp Trp Val Ser Val Pro Val
9475 9480 9485

ccc gcc aac gcc cct tcg ccc acc gcg gac cgg ccc tgg gcg gtc atc 28566
Pro Ala Asn Ala Pro Ser Pro Thr Ala Asp Arg Pro Trp Ala Val Ile
9490 9495 9500

ggc gcg ggc ctt ccc cac ctg ccc ggc ctg acg gag cac gag cac gtg 28614
Gly Ala Gly Leu Pro His Leu Pro Gly Leu Thr Glu His Glu His Val
9505 9510 9515 9520

acc gcg tat gac gag ccg gcg gac ctg ctt ctg gct ctg gac cgc ggt 28662
Thr Ala Tyr Asp Glu Pro Ala Asp Leu Leu Leu Ala Leu Asp Arg Gly
9525 9530 9535

gct ccg ccg ccc ggt gtg ctg gtc gta ggt ggt gtc gcc cac acc gaa 28710
Ala Pro Pro Pro Gly Val Leu Val Val Gly Gly Val Ala His Thr Glu
9540 9545 9550

gcc cgg gag tat tcc gcc gaa gcc ccc ggg gag cgc ggg acc gag gcc 28758
Ala Arg Glu Tyr Ser Ala Glu Ala Pro Gly Glu Arg Gly Thr Glu Ala
9555 9560 9565

tgc gag gcc cgg ccg gac gtc gtg cac gtg ggc gtc gtg cac acg gct 28806
Cys Glu Ala Arg Pro Asp Val Val His Val Gly Val Val His Thr Ala
9570 9575 9580

gcc gtg cac gcg gct gcc gcg cag atg ttg gcc agg ctc cag gcc tgg 28854
Ala Val His Ala Ala Ala Ala Gln Met Leu Ala Arg Leu Gln Ala Trp
9585 9590 9595 9600

ctg ggc gac gag cgc ctc gca gac agc cgg ctg ctc gtc ctg acg tgc 28902
Leu Gly Asp Glu Arg Leu Ala Asp Ser Arg Leu Leu Val Leu Thr Cys
9605 9610 9615

ggc gcg gtc gcc cgc gcc tcc ggc gac gat gcg acg gac ctg ccc ggg 28950
Gly Ala Val Ala Arg Ala Ser Gly Asp Asp Ala Thr Asp Leu Pro Gly
9620 9625 9630

gcc gcc gtg tgg ggg ctg gtg cgt tcg gcg cag tcc gag cac ccg gac 28998
Ala Ala Val Trp Gly Leu Val Arg Ser Ala Gln Ser Glu His Pro Asp
9635 9640 9645

cgc atc acg ctg ctg gac ttc gag cgg ggc aca gag gcg gag ccc ggt 29046
Arg Ile Thr Leu Leu Asp Phe Glu Arg Gly Thr Glu Ala Glu Pro Gly
9650 9655 9660

cag ctg gcg acg gcg ctg aac tgc ggg gag cgg cag ctt gcc gtc cgc 29094
Gln Leu Ala Thr Ala Leu Asn Cys Gly Glu Arg Gln Leu Ala Val Arg
9665 9670 9675 9680

ccc gga ggg ctg ttc acg cca cgg ctg gtg cgc gcg cca cgt gtc gcc 29142
Pro Gly Gly Leu Phe Thr Pro Arg Leu Val Arg Ala Pro Arg Val Ala
9685 9690 9695

gac gcc gta ccc gcc gta ccc gcc gtg gcc gta ccg tca gcg ggt cac 29190
Asp Ala Val Pro Ala Val Pro Ala Val Ala Val Pro Ser Ala Gly His
9700 9705 9710

gca gcc gta ccg gca gcg ggt ccc ttc ctt ccg ggc gga acg gtg ctg 29238
Ala Ala Val Pro Ala Ala Gly Pro Phe Leu Pro Gly Gly Thr Val Leu
9715 9720 9725

atc acc ggc gga acc ggt gtc ctg ggc cgg ctc gtg gcc cgg cat ctg 29286

Ile Thr Gly Gly Thr Gly Val Leu Gly Arg Leu Val Ala Arg His Leu
9730 9735 9740

gtg gag gcg cac ggc gta cgg cat ctg ttg ctg gcg ggt cgg cgc gga 29334
Val Glu Ala His Gly Val Arg His Leu Leu Leu Ala Gly Arg Arg Gly
9745 9750 9755 9760

ccg gac gcc gag ggt gcg ccg gag ttg cgg gcg gag ctc ggt ggg ctc 29382
Pro Asp Ala Glu Gly Ala Pro Glu Leu Arg Ala Glu Leu Gly Gly Leu
9765 9770 9775

ggc gcg acg gtg gag gtc gtc gcc tgc gac gcg gcg gac cgg cag cag 29430
Gly Ala Thr Val Glu Val Val Ala Cys Asp Ala Ala Asp Arg Gln Gln
9780 9785 9790

ctg gcc gac ctg ctg aca cgg atc ccc gac gat cgg ccg ctg acc ggt 29478
Leu Ala Asp Leu Leu Thr Arg Ile Pro Asp Asp Arg Pro Leu Thr Gly
9795 9800 9805

gtc gtg cac agt gcg ggc atc ctg gac gac ggc gtg atc acg tcg ctg 29526
Val Val His Ser Ala Gly Ile Leu Asp Asp Gly Val Ile Thr Ser Leu
9810 9815 9820

tcg ccg gag cgg ctc ggg gcc gtc ctc cgg gcc aag gcg gac gct gcg 29574
Ser Pro Glu Arg Leu Gly Ala Val Leu Arg Ala Lys Ala Asp Ala Ala
9825 9830 9835 9840

ctg ctt ctc gac gag ctg acg cgc ggg gca gag ctg tcg gct ttc gtc 29622
Leu Leu Leu Asp Glu Leu Thr Arg Gly Ala Glu Leu Ser Ala Phe Val
9845 9850 9855

atg ttc tcc tcc gcg tcg gcg gtg gtc ggc tcg ccc ggg cag ggc aac 29670
Met Phe Ser Ser Ala Ser Ala Val Val Gly Ser Pro Gly Gln Gly Asn
9860 9865 9870

tac gcc gcc gcc aac gcc gtc ctc gac ttc ctt gct cat cgc cgc cgc 29718
Tyr Ala Ala Ala Asn Ala Val Leu Asp Phe Leu Ala His Arg Arg Arg
9875 9880 9885

gcc gag ggg ctg ccc gcc gtc tct ctc gcc tgg ggc ctg tgg gaa gag 29766
Ala Glu Gly Leu Pro Ala Val Ser Leu Ala Trp Gly Leu Trp Glu Glu
9890 9895 9900

ggc aca ggg atg acg ggc cac ctc gac gtc gac gac cat gcg cgg atc 29814
Gly Thr Gly Met Thr Gly His Leu Asp Val Asp Asp His Ala Arg Ile
9905 9910 9915 9920

agc cgc gcg gga atg cgg ccg ctg ccg act gcc gag gct ctg gcg ctg 29862
Ser Arg Ala Gly Met Arg Pro Leu Pro Thr Ala Glu Ala Leu Ala Leu
9925 9930 9935

ttc gac gcg gcc ttg gcc gac ggc gag ccg ttc ctg atg ccg gct cgg 29910
Phe Asp Ala Ala Leu Ala Asp Gly Glu Pro Phe Leu Met Pro Ala Arg
9940 9945 9950

ctc gac ctc acg gcc gta cgg tct ggt gcc gcg tcc gca ccg gtg ccg 29958
Leu Asp Leu Thr Ala Val Arg Ser Gly Ala Ala Ser Ala Pro Val Pro
9955 9960 9965

ccg ctg ctg caa ggt ctg ctt cag ctg cct cgg tcc cgc tcg gcc gcc 30006
Pro Leu Leu Gln Gly Leu Leu Gln Leu Pro Arg Ser Arg Ser Ala Ala
9970 9975 9980

gcg gcc ccc ggc cat ggg gcc ccg gcg gcg gac gag gcg gcg gcc tgg 30054
Ala Ala Pro Gly His Gly Ala Pro Ala Ala Asp Glu Ala Ala Ala Trp
9985 9990 9995 10000

cgt gag cgt ctg gcc cgg cag agt gcc ggt gag cgc agg cag gcg ctg 30102
Arg Glu Arg Leu Ala Arg Gln Ser Ala Gly Glu Arg Arg Gln Ala Leu
10005 10010 10015

ctg cgc ctg gtg cgg tcg cat gtc gcg gcg gtg ctc ggc cat agc ggt 30150
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Val Asn Gln Asp Gly Ala Ser Asn Gly Leu Thr Ala Pro Asn Gly Pro
1860 1865 1870

tcg cag cag cgg gtg att cgg cag gcg ttg gcg tgt gcg ggg ttg tcc 5664
Ser Gln Gln Arg Val Ile Arg Gln Ala Leu Ala Cys Ala Gly Leu Ser

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1875 1880 1885

gtg gcg gat gtg gat gtg gtg gag ggg cac ggg acg ggt acg acg ttg 5712
Val Ala Asp Val Asp Val Val Glu Gly His Gly Thr Gly Thr Thr Leu
1890 1895 1900

ggt gat ccg atc gag gcg cag gcg ttg ctc gcc act tat ggg cag ggt 5760
Gly Asp Pro Ile Glu Ala Gln Ala Leu Leu Ala Thr Tyr Gly Gln Gly
1905 1910 1915 1920

cgt tcg ggg gag cgg ccg gtg tgg ttg ggg tcg gtg aag tcg aac atc 5808
Arg Ser Gly Glu Arg Pro Val Trp Leu Gly Ser Val Lys Ser Asn Ile
1925 1930 1935

ggg cat gcg cag gct gct gcg ggt gtg gcg ggt gtg atc aag atg gtg 5856
Gly His Ala Gln Ala Ala Ala Gly Val Ala Gly Val Ile Lys Met Val
1940 1945 1950

atg gcg ttg cgg gcg ggg gtg ttg ccg cgg acg ttg cat gtg gat gag 5904
Met Ala Leu Arg Ala Gly Val Leu Pro Arg Thr Leu His Val Asp Glu
1955 1960 1965

ccg tcg tcg cag gtg gat tgg tcg agt ggg tcg gtt cgt gtg ttg gcg 5952
Pro Ser Ser Gln Val Asp Trp Ser Ser Gly Ser Val Arg Val Leu Ala
1970 1975 1980

gat gag gtg gag tgg ccg ggg gtg gag ggt cgg ctg cgg cgt gcg ggg 6000
Asp Glu Val Glu Trp Pro Gly Val Glu Gly Arg Leu Arg Arg Ala Gly
1985 1990 1995 2000

gtg tct gcg ttc ggg gtg agt ggg acg aat gcg cat gtg att ttg gag 6048
Val Ser Ala Phe Gly Val Ser Gly Thr Asn Ala His Val Ile Leu Glu
2005 2010 2015

gag gcg tcc ggg ggc gcg gat ggg ggt gcg ggc cgg ctg cag gag ttg 6096
Glu Ala Ser Gly Gly Ala Asp Gly Gly Ala Gly Arg Leu Gln Glu Leu
2020 2025 2030

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ggt ccg ggg gtg gtg tcg ggt tcg ggg gtg gtg ccg tgg gtg gtg tcg 6144
Gly Pro Gly Val Val Ser Gly Ser Gly Val Val Pro Trp Val Val Ser
2035 2040 2045

gcg cgg tcg gag ttg gcg ttg cgg ggg cag gcg cgt cgg ttg cgt ggg 6192
Ala Arg Ser Glu Leu Ala Leu Arg Gly Gln Ala Arg Arg Leu Arg Gly
2050 2055 2060

gtt gtg gcg gtt ggt ggg ggt gcg gat ggt gtg ggg gtg agt ccg gct 6240
Val Val Ala Val Gly Gly Gly Ala Asp Gly Val Gly Val Ser Pro Ala
2065 2070 2075 2080

ggg gtc ggg cgg gct ttg gtg tcg gag cgg tcg gtg ttc gag cat cgt 6288
Gly Val Gly Arg Ala Leu Val Ser Glu Arg Ser Val Phe Glu His Arg
2085 2090 2095

gcg gtg gtc gtg gcc gag gac cgc gac gag ttc ctg cac gca ctc gac 6336
Ala Val Val Val Ala Glu Asp Arg Asp Glu Phe Leu His Ala Leu Asp
2100 2105 2110

gca ctg gcc gag ggg gca ccc acc gcg ggg gtg gta cag ggt gtg gcc 6384
Ala Leu Ala Glu Gly Ala Pro Thr Ala Gly Val Val Gln Gly Val Ala
2115 2120 2125

gga ccg gcg gcc gac gga aag atc gcc atg ctg ttc gga gga cag ggc 6432
Gly Pro Ala Ala Asp Gly Lys Ile Ala Met Leu Phe Gly Gly Gln Gly
2130 2135 2140

acc cac tgg gaa ggc atg gcg cag gaa ctc ctc ggc tcc tca ccg gtc 6480
Thr His Trp Glu Gly Met Ala Gln Glu Leu Leu Gly Ser Ser Pro Val
2145 2150 2155 2160

ttc gcc cag cag atg tcc gac tgc gcc caa gcc ctc gaa ccg tac ctg 6528
Phe Ala Gln Gln Met Ser Asp Cys Ala Gln Ala Leu Glu Pro Tyr Leu
2165 2170 2175

gac tgg tct ctc ctc gac gtc ctg cgc ggc gca ccg gac gca ccc cct 6576
Asp Trp Ser Leu Leu Asp Val Leu Arg Gly Ala Pro Asp Ala Pro Pro

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2180 2185 2190

ctg caa cgc gtc gat gtc gtc cag ccc gtc ctc ttc gcg gtg atg gtc 6624
Leu Gln Arg Val Asp Val Val Gln Pro Val Leu Phe Ala Val Met Val
2195 2200 2205

tcg ctg gcg gcg ctc tgg cgc tcg tac ggt gta cac ccg gac gcg gtg 6672
Ser Leu Ala Ala Leu Trp Arg Ser Tyr Gly Val His Pro Asp Ala Val
2210 2215 2220

gcc ggg cac tcg cag ggc gag atc gca gcg gcc tac gtc gcc ggt gca 6720
Ala Gly His Ser Gln Gly Glu Ile Ala Ala Ala Tyr Val Ala Gly Ala
2225 2230 2235 2240

ctc tcc ctc gac gac gcc gcc cgg gtc acc gcc ctg cgc agc cag gcg 6768
Leu Ser Leu Asp Asp Ala Ala Arg Val Thr Ala Leu Arg Ser Gln Ala
2245 2250 2255

ctg gcc gca ctg gcc ggg cag ggg gcg atg gca tcg gtc ggt ctg ccg 6816
Leu Ala Ala Leu Ala Gly Gln Gly Ala Met Ala Ser Val Gly Leu Pro
2260 2265 2270

gtc gag aag ctg gag ccg cgt ctt gcg aca tgg ggc gac cgt ctg gtc 6864
Val Glu Lys Leu Glu Pro Arg Leu Ala Thr Trp Gly Asp Arg Leu Val
2275 2280 2285

atc gcc gcc gtg aac ggg gcg cgt tcg gcc gtg gtc tcc ggg gag ccg 6912
Ile Ala Ala Val Asn Gly Ala Arg Ser Ala Val Val Ser Gly Glu Pro
2290 2295 2300

gaa gcg gtc gac gcc ctg gtg gag gag ctg tca cac gaa gac gta ccg 6960
Glu Ala Val Asp Ala Leu Val Glu Glu Leu Ser His Glu Asp Val Pro
2305 2310 2315 2320

gcc cgc agg ctc atg gtc gac tgg gcg tcg cac tcc ccg cag gtc gag 7008
Ala Arg Arg Leu Met Val Asp Trp Ala Ser His Ser Pro Gln Val Glu
2325 2330 2335

gcg atc cag ggg cgg ctg ctc gaa ctc ctc gcc ccc atc cgc gcg agg 7056
Ala Ile Gln Gly Arg Leu Leu Glu Leu Leu Ala Pro Ile Arg Ala Arg
2340 2345 2350

acc ggc gac gtg ccc ttc tac tcc acc gtc acc ggc gaa cgc atc gac 7104
Thr Gly Asp Val Pro Phe Tyr Ser Thr Val Thr Gly Glu Arg Ile Asp
2355 2360 2365

ggc acc gaa ctc gac gcc gac tac tgg tac cgc aac ctg cgc cag gtc 7152
Gly Thr Glu Leu Asp Ala Asp Tyr Trp Tyr Arg Asn Leu Arg Gln Val
2370 2375 2380

gtc cgc ttc cgg gac gcg aca cag gcg ctg gtc cgc gcc ggc cac acc 7200
Val Arg Phe Arg Asp Ala Thr Gln Ala Leu Val Arg Ala Gly His Thr
2385 2390 2395 2400

gtc ttc atc gag gcg tgc ccg cat ccg gcc gtc gcg gtc ggt gtg cag 7248
Val Phe Ile Glu Ala Cys Pro His Pro Ala Val Ala Val Gly Val Gln
2405 2410 2415

gaa acc ctg gac gag atg ggt gac ttg gac agc ctg gtc gtc gga tct 7296
Glu Thr Leu Asp Glu Met Gly Asp Leu Asp Ser Leu Val Val Gly Ser
2420 2425 2430

ctg cgc cgg ggc gaa ggc ggc ttg cga cgc ttc ctg atg tcc gtg gcc 7344
Leu Arg Arg Gly Glu Gly Gly Leu Arg Arg Phe Leu Met Ser Val Ala
2435 2440 2445

gag ttg ttc gtg ggt ggg gtg gcg gtt gag tgg tcc ggt gtg ttc ggg 7392
Glu Leu Phe Val Gly Gly Val Ala Val Glu Trp Ser Gly Val Phe Gly
2450 2455 2460

agt gtt ggt cgc ggg gtc gct ggt ggt tgc ggg gtg gag ctg ccg acg 7440
Ser Val Gly Arg Gly Val Ala Gly Gly Cys Gly Val Glu Leu Pro Thr
2465 2470 2475 2480

tat gcg ttc gag cga gag cgc ttt tgg ctg gat gtg gag ggg gcg ccg 7488
Tyr Ala Phe Glu Arg Glu Arg Phe Trp Leu Asp Val Glu Gly Ala Pro

cgg ggt tcc ggg gtc tct ggg cag tgg ggt ggt cag ttg tcg gag gcg 7536
Arg Gly Ser Gly Val Ser Gly Gln Trp Gly Gly Gln Leu Ser Glu Ala
2500 2505 2510

gtg gac acc gtg cgc ggc ggc atg ctg cgc gac tgc ctc gcc gga ctc 7584
Val Asp Thr Val Arg Gly Gly Met Leu Arg Asp Cys Leu Ala Gly Leu
2515 2520 2525

gac ccc gcc gca cag gcc gag acc gtg ctg gac ctg gtc ctt acc cat 7632
Asp Pro Ala Ala Gln Ala Glu Thr Val Leu Asp Leu Val Leu Thr His
2530 2535 2540

gcc gcg gcc gtc ctt gga cac ggc acc gcc gat gcg gtg gtg ccc gag 7680
Ala Ala Ala Val Leu Gly His Gly Thr Ala Asp Ala Val Val Pro Glu
2545 2550 2555 2560

cgc gcc ttc cgc gac ctc ggt ttc gac tcc ctc acc gcc gtc gaa cta 7728
Arg Ala Phe Arg Asp Leu Gly Phe Asp Ser Leu Thr Ala Val Glu Leu
2565 2570 2575

cgc aac cgc ctc aac acc gcc acg ggc ctg cgc ttc ccg agg acc ctg 7776
Arg Asn Arg Leu Asn Thr Ala Thr Gly Leu Arg Phe Pro Arg Thr Leu
2580 2585 2590

gtg ttc gac cat ccc cgc ccg gtg gca ctc gcg gca cac atc cac gag 7824
Val Phe Asp His Pro Arg Pro Val Ala Leu Ala Ala His Ile His Glu
2595 2600 2605

cag ctg agc ggc gga agc ccg acc acc ggc act gcc ctt gcc ctt gcc 7872
Gln Leu Ser Gly Gly Ser Pro Thr Thr Gly Thr Ala Leu Ala Leu Ala
2610 2615 2620

ctt cgg gcc ccg gca ccg cgt gtg gat gtc gac gag ccg att gcc att 7920
Leu Arg Ala Pro Ala Pro Arg Val Asp Val Asp Glu Pro Ile Ala Ile
2625 2630 2635 2640

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gtg ggg atg gcg tgc cgt ttt ccg ggg ggt gtg gag tcg gcg gag gat 7968
Val Gly Met Ala Cys Arg Phe Pro Gly Gly Val Glu Ser Ala Glu Asp
2645 2650 2655

ttc tgg gag ttg atc gcg tcg ggt cgg gat gcg gtg ggg gag ttt ccg 8016
Phe Trp Glu Leu Ile Ala Ser Gly Arg Asp Ala Val Gly Glu Phe Pro
2660 2665 2670

gtc gac cgg ggt tgg gac gtg gag gct ttc tat gat ccg gag ccg ggg 8064
Val Asp Arg Gly Trp Asp Val Glu Ala Phe Tyr Asp Pro Glu Pro Gly
2675 2680 2685

cgg gcg ggt acg tcc tac acg cgg tgt ggt ggg ttt ttg cag ggt gcg 8112
Arg Ala Gly Thr Ser Tyr Thr Arg Cys Gly Gly Phe Leu Gln Gly Ala
2690 2695 2700

gcg gag ttc gat gcg ggg ttt ttc ggg atc agt ccg cgt gag gcg ttg 8160
Ala Glu Phe Asp Ala Gly Phe Phe Gly Ile Ser Pro Arg Glu Ala Leu
2705 2710 2715 2720

gcg atg gat ccg cag cag cgg ttg atg ctg gag gtg tcc tgg gag gcg 8208
Ala Met Asp Pro Gln Gln Arg Leu Met Leu Glu Val Ser Trp Glu Ala
2725 2730 2735

ttg gag cgg gcg ggc atc gac ccc gcc acg ctg cac ggg tcc acg acc 8256
Leu Glu Arg Ala Gly Ile Asp Pro Ala Thr Leu His Gly Ser Thr Thr
2740 2745 2750

ggt gtc ttc gcc ggc gtc tcg cag cag gac tac gcc gag ctc ctg cgc 8304
Gly Val Phe Ala Gly Val Ser Gln Gln Asp Tyr Ala Glu Leu Leu Arg
2755 2760 2765

cgc ggc acc cag gac cac gag ggg tac gcg ctc acc ggc gtc tcc aac 8352
Arg Gly Thr Gln Asp His Glu Gly Tyr Ala Leu Thr Gly Val Ser Asn
2770 2775 2780

agc gtc gtc tcc ggg cgg ctt tcc tac acc ttc ggc ttc gag ggt ccg 8400
Ser Val Val Ser Gly Arg Leu Ser Tyr Thr Phe Gly Phe Glu Gly Pro

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WO 2004/050696 PCT/US2003/038474

2785 2790 2795 2800

gcg gtg acg gtg gat acg gcg tgt tcg tcg tcg ttg gtg gcg ctg cat 8448
Ala Val Thr Val Asp Thr Ala Cys Ser Ser Ser Leu Val Ala Leu His
2805 2810 2815

ctg gcg tgt cag gcg ttg agg tcg ggg gag tgt tcg ctg gcg ttg gcg 8496
Leu Ala Cys Gln Ala Leu Arg Ser Gly Glu Cys Ser Leu Ala Leu Ala
2820 2825 2830

ggg ggt gtg acg gtg atg tcg acg ccg ggt gcg ttt gtg gag ttc tcg 8544
Gly Gly Val Thr Val Met Ser Thr Pro Gly Ala Phe Val Glu Phe Ser
2835 2840 2845

cgg cag cgg ggt ctg tcg ccg gac ggc cgg tgc aag gcg tac ggg tcg 8592
Arg Gln Arg Gly Leu Ser Pro Asp Gly Arg Cys Lys Ala Tyr Gly Ser
2850 2855 2860

ggg gcc gat ggg gtc ggc tgg gcc gag ggt gtg ggt gtg ctg ttg gtg 8640
Gly Ala Asp Gly Val Gly Trp Ala Glu Gly Val Gly Val Leu Leu Val
2865 2870 2875 2880

gag cgg ctg tcc gag gct gaa cgt cgt ggt cat cgg gtt ttg gcg gtg 8688
Glu Arg Leu Ser Glu Ala Glu Arg Arg Gly His Arg Val Leu Ala Val
2885 2890 2895

gtg cgg ggg agt gcg gtg aat cag gac ggt gcg tcg aat ggg ttg acg 8736
Val Arg Gly Ser Ala Val Asn Gln Asp Gly Ala Ser Asn Gly Leu Thr
2900 2905 2910

gcg ccg aat ggt ccg tcg cag cag cgg gtg att cgg cag gcg ttg gcg 8784
Ala Pro Asn Gly Pro Ser Gln Gln Arg Val Ile Arg Gln Ala Leu Ala
2915 2920 2925

tgt gcg ggg ttg tcc gtg gcg gat gtg gat gtg gtg gag ggg cac ggg 8832
Cys Ala Gly Leu Ser Val Ala Asp Val Asp Val Val Glu Gly His Gly
2930 2935 2940

acg ggt acg acg ttg ggt gat ccg atc gag gcg cag gcg ttg ctc gcc 8880
Thr Gly Thr Thr Leu Gly Asp Pro Ile Glu Ala Gln Ala Leu Leu Ala
2945 2950 2955 2960

acg tac ggg cag ggt cgt tcg ggg gag cgg ccg gtg tgg ttg ggg tcg 8928
Thr Tyr Gly Gln Gly Arg Ser Gly Glu Arg Pro Val Trp Leu Gly Ser
2965 2970 2975

gtg aag tcg aac atc ggg cat gcg cag gct gcc gcg ggt gtg gcc ggt 8976
Val Lys Ser Asn Ile Gly His Ala Gln Ala Ala Ala Gly Val Ala Gly
2980 2985 2990

gtg atc aag atg gtc atg gcc ctg aac cac gaa ctg ttg ccg acc agc 9024
Val Ile Lys Met Val Met Ala Leu Asn His Glu Leu Leu Pro Thr Ser
2995 3000 3005

ctg cac atc gac gaa ccc tcc ccc cac atc gac tgg tcg agc ggc ggc 9072
Leu His Ile Asp Glu Pro Ser Pro His Ile Asp Trp Ser Ser Gly Gly
3010 3015 3020

gtc cgg ctt ctc acc gag ccc gta ccg tgg cag cag aac ggc cgg ccc 9120
Val Arg Leu Leu Thr Glu Pro Val Pro Trp Gln Gln Asn Gly Arg Pro
3025 3030 3035 3040

agg cgc gcg ggc gtc tcc gcg ttc gga gtc agc ggg acc aac gcc cac 9168
Arg Arg Ala Gly Val Ser Ala Phe Gly Val Ser Gly Thr Asn Ala His
3045 3050 3055

gtc atc atc gag cag gcg ccg gtc gag gcg cac gtc atc agt gag ccg 9216
Val Ile Ile Glu Gln Ala Pro Val Glu Ala His Val Ile Ser Glu Pro
3060 3065 3070

gta ccg gct gag gcg cac gtc atc gtc gag cag gcg ccg gtc gag gcg 9264
Val Pro Ala Glu Ala His Val Ile Val Glu Gln Ala Pro Val Glu Ala
3075 3080 3085

ccc cac gtg gtc gac gcc acc gga ccg gcg gac ctc acc gag ccg caa 9312
Pro His Val Val Asp Ala Thr Gly Pro Ala Asp Leu Thr Glu Pro Gln

Replacement Sheet

3090 3095 3100

gag gag gcg gct gaa ccg gag tgc gtc gct gac gcc gtg acc gag atg 9360
Glu Glu Ala Ala Glu Pro Glu Cys Val Ala Asp Ala Val Thr Glu Met
3105 3110 3115 3120

tcg gct gaa ccg gag tgc gtc gcc gac gcc atg tcc gag atg tcg gct 9408
Ser Ala Glu Pro Glu Cys Val Ala Asp Ala Met Ser Glu Met Ser Ala
3125 3130 3135

gag tgc gtc gcc gag gcc gtg tcc gac aag tcg gct gaa ccg gag tgc 9456
Glu Cys Val Ala Glu Ala Val Ser Asp Lys Ser Ala Glu Pro Glu Cys
3140 3145 3150

gtc gcc gac gcc atg tcc gac aag ccg gcc ctc ctg ccc atc ccg tgg 9504
Val Ala Asp Ala Met Ser Asp Lys Pro Ala Leu Leu Pro Ile Pro Trp
3155 3160 3165

ctg ctc tcc gcc aag tcc gag cga gcg ctg cgg ggc cag gcg cga cgg 9552
Leu Leu Ser Ala Lys Ser Glu Arg Ala Leu Arg Gly Gln Ala Arg Arg
3170 3175 3180

ttg cgg cag ttc gct gcc agg gca tcc gat gcc cgg ccg gcc gac gtg 9600
Leu Arg Gln Phe Ala Ala Arg Ala Ser Asp Ala Arg Pro Ala Asp Val
3185 3190 3195 3200

gcg cac gcc ctg gcg gca cag cgg tcc gtg ttc gat cac cgg gcc gtc 9648
Ala His Ala Leu Ala Ala Gln Arg Ser Val Phe Asp His Arg Ala Val
3205 3210 3215

gtc gtg gcc gag gac cgc gac ggc ttc ctt cag gcc ctc gac gcg ctg 9696
Val Val Ala Glu Asp Arg Asp Gly Phe Leu Gln Ala Leu Asp Ala Leu
3220 3225 3230

gcc gag ggc cgg tcg gcg gac ggc ctg atc gaa ggg tcg gtc ggc ccg 9744
Ala Glu Gly Arg Ser Ala Asp Gly Leu Ile Glu Gly Ser Val Gly Pro
3235 3240 3245

cgt ggc ggc cac tca ggc cgc cgg cgc gga aag acc gcc atg ctg ttc 9792
Arg Gly Gly His Ser Gly Arg Arg Arg Gly Lys Thr Ala Met Leu Phe
3250 3255 3260

gcc gga cag ggc acg caa cgc gtg gga atg ggc cgt cag ctg tat gcg 9840
Ala Gly Gln Gly Thr Gln Arg Val Gly Met Gly Arg Gln Leu Tyr Ala
3265 3270 3275 3280

gct cac ccg gcc tac gcg gac gcg ctg gac cag gta ctg gcg gaa ctg 9888
Ala His Pro Ala Tyr Ala Asp Ala Leu Asp Gln Val Leu Ala Glu Leu
3285 3290 3295

gac ggt cac ctg gac cag ccc ctg cgc ccg ctg atc cac gcc agt gcg 9936
Asp Gly His Leu Asp Gln Pro Leu Arg Pro Leu Ile His Ala Ser Ala
3300 3305 3310

gat ctt gcg gat gtc gcg gat gcc gcg gat gtt ctg gac cgt acg cgg 9984
Asp Leu Ala Asp Val Ala Asp Ala Ala Asp Val Leu Asp Arg Thr Arg
3315 3320 3325

tac gcc cag ccg gcg ctg ttc gcc gtc cag gtc gcg ctc ttc cgg cac 10032
Tyr Ala Gln Pro Ala Leu Phe Ala Val Gln Val Ala Leu Phe Arg His
3330 3335 3340

ctg gaa cgt ctc ggc gtg cgc gcg gac ttc gtg gcc ggg cac tcg atc 10080
Leu Glu Arg Leu Gly Val Arg Ala Asp Phe Val Ala Gly His Ser Ile
3345 3350 3355 3360

ggc gag ctc gcg gcc gcc cac gtc gcc ggg gtg ctt ccc ctg gca gca 10128
Gly Glu Leu Ala Ala Ala His Val Ala Gly Val Leu Pro Leu Ala Ala
3365 3370 3375

gcc tgc cgc ctg gtg gcg gcc cgc ggg cgc ctg atg gag cag ctc gca 10176
Ala Cys Arg Leu Val Ala Ala Arg Gly Arg Leu Met Glu Gln Leu Ala
3380 3385 3390

cca ggc ggc gcc atg gtc gcc gta cgg gcg agc gaa gcc gag gcg cga 10224
Pro Gly Gly Ala Met Val Ala Val Arg Ala Ser Glu Ala Glu Ala Arg

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3395 3400 3405

cag gcg ctc gac ggc cgg gaa gcc cgg gtg tcg gtc gcg gcc gtg aac 10272
Gln Ala Leu Asp Gly Arg Glu Ala Arg Val Ser Val Ala Ala Val Asn
3410 3415 3420

gga ccc gcc tcg gtg gtg ttc tcc ggc gcc gag gac gag gtg ggg aac 10320
Gly Pro Ala Ser Val Val Phe Ser Gly Ala Glu Asp Glu Val Gly Asn
3425 3430 3435 3440

atg gcg gac tgg ttc gcc gag cgc ggg cgg aga gtc aag cgc ctg cga 10368
Met Ala Asp Trp Phe Ala Glu Arg Gly Arg Arg Val Lys Arg Leu Arg
3445 3450 3455

acc ggg cat gcc ttc cac tca ccg ctg atg gac ccg atg ctg gag gag 10416
Thr Gly His Ala Phe His Ser Pro Leu Met Asp Pro Met Leu Glu Glu
3460 3465 3470

ttc cag cag gtc gcg gcc tcg ctg acc tac agc gaa cca gcc att ccc 10464
Phe Gln Gln Val Ala Ala Ser Leu Thr Tyr Ser Glu Pro Ala Ile Pro
3475 3480 3485

atg gtg tcg acg ctc acc ggc gac atc gtg gcg gcg gga gaa ctg agc 10512
Met Val Ser Thr Leu Thr Gly Asp Ile Val Ala Ala Gly Glu Leu Ser
3490 3495 3500

gac ccc gag tac tgg gtc cgg cag gta cgg cgg acc gtg cgc ttc ggc 10560
Asp Pro Glu Tyr Trp Val Arg Gln Val Arg Arg Thr Val Arg Phe Gly
3505 3510 3515 3520

gac gcg atc agc cgc ctg cac acc gac gga gtc cgc acc ttc atg gaa 10608
Asp Ala Ile Ser Arg Leu His Thr Asp Gly Val Arg Thr Phe Met Glu
3525 3530 3535

ctg ggc cca gac ggg acc ctg tcg gca ctg gcc gag gaa tgc cta gag 10656
Leu Gly Pro Asp Gly Thr Leu Ser Ala Leu Ala Glu Glu Cys Leu Glu
3540 3545 3550

gcc acc gcc gac agc cac ccc gcc gac gac gac acc ggc acc ccg caa 10704
Ala Thr Ala Asp Ser His Pro Ala Asp Asp Asp Thr Gly Thr Pro Gln
3555 3560 3565

gag aac ctg ctc atc ccg ctc cta cgg ccg gac agc ccg gaa ccc ggc 10752
Glu Asn Leu Leu Ile Pro Leu Leu Arg Pro Asp Ser Pro Glu Pro Gly
3570 3575 3580

acc ctg ctc acc ggc ttg gcc cgg ctg cat acg cac gga gcg gcg gcg 10800
Thr Leu Leu Thr Gly Leu Ala Arg Leu His Thr His Gly Ala Ala Ala
3585 3590 3595 3600

gtc aac tgg ccc gcc gcc ctg ccc gaa cgc gat cga gcc cgc cac ctc 10848
Val Asn Trp Pro Ala Ala Leu Pro Glu Arg Asp Arg Ala Arg His Leu
3605 3610 3615

gac ctg ccg acc tac gcc ttc gat cac cac cgc tac tgg gtc gac acc 10896
Asp Leu Pro Thr Tyr Ala Phe Asp His His Arg Tyr Trp Val Asp Thr
3620 3625 3630

tcg gcc ggc cac ccg ggg gac ctg tcg gca gcg ggg ctc ggc acc gcc 10944
Ser Ala Gly His Pro Gly Asp Leu Ser Ala Ala Gly Leu Gly Thr Ala
3635 3640 3645

ggg cat ccc ctg ctc ggt tcc gcg gtg gca ctg gcc gag tcg cag gaa 10992
Gly His Pro Leu Leu Gly Ser Ala Val Ala Leu Ala Glu Ser Gln Glu
3650 3655 3660

ctc ctc ttc acc ggc cgt ctc tcc ctg cgc aca cac ccg tgg ctg gcc 11040
Leu Leu Phe Thr Gly Arg Leu Ser Leu Arg Thr His Pro Trp Leu Ala
3665 3670 3675 3680

gac cac gcc atc ttc ggt acc gtc ctg ctg ccc ggc acg gcc atc ctg 11088
Asp His Ala Ile Phe Gly Thr Val Leu Leu Pro Gly Thr Ala Ile Leu
3685 3690 3695

gaa ctg gcc gtg cgc gca ggc gac gag gtc gac tgc ggc acc gtc gag 11136
Glu Leu Ala Val Arg Ala Gly Asp Glu Val Asp Cys Gly Thr Val Glu

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3700 3705 3710

gaa ctc acc ctg cgg aca ccg ctc gtc ctt ccc gaa cag ggc tcg gtg 11184
Glu Leu Thr Leu Arg Thr Pro Leu Val Leu Pro Glu Gln Gly Ser Val
3715 3720 3725

atc ctg caa ctc tcc gtc ggg gca ccc cag ggc ccc cag acg ccc gag 11232
Ile Leu Gln Leu Ser Val Gly Ala Pro Gln Gly Pro Gln Thr Pro Glu
3730 3735 3740

gag ccc gaa cgg cgc acc ttc gcc ctg tac gcc cgc gaa gac gac gga 11280
Glu Pro Glu Arg Arg Thr Phe Ala Leu Tyr Ala Arg Glu Asp Asp Gly
3745 3750 3755 3760

ctg tcg tcc tcg tcc gcg gcg gcg acc ggc acc gag tgg acc tgc cac 11328
Leu Ser Ser Ser Ser Ala Ala Ala Thr Gly Thr Glu Trp Thr Cys His
3765 3770 3775

gcc acc ggc gtc ctg acc ggc acc gcc cgg ccc gcg gag gag cac aca 11376
Ala Thr Gly Val Leu Thr Gly Thr Ala Arg Pro Ala Glu Glu His Thr
3780 3785 3790

cag gaa ccg tgg ccg ccc gcc gac gca gca ccg gtg gac ctg gac ggc 11424
Gln Glu Pro Trp Pro Pro Ala Asp Ala Ala Pro Val Asp Leu Asp Gly
3795 3800 3805

tgg tac gag cag ctg gcc ggc gcc ggc ctg gga tac ggg ccg gtg ttc 11472
Trp Tyr Glu Gln Leu Ala Gly Ala Gly Leu Gly Tyr Gly Pro Val Phe
3810 3815 3820

cag ggg ctg cgc gag gtc tgg cgg cgc ggg gac gag gtg ttc gcc gtc 11520
Gln Gly Leu Arg Glu Val Trp Arg Arg Gly Asp Glu Val Phe Ala Val
3825 3830 3835 3840

gtc acc ctg ccc gag agc acg gag gga cag gcg gcc gac gcc gcc cgg 11568
Val Thr Leu Pro Glu Ser Thr Glu Gly Gln Ala Ala Asp Ala Ala Arg
3845 3850 3855

tac gcc ctg cac ccg gcc ctg ctg gac gcg gca ctg cac ccg gtc gtt 11616
Tyr Ala Leu His Pro Ala Leu Leu Asp Ala Ala Leu His Pro Val Val
3860 3865 3870

ctg cgc cac gag ggc gat gcc gcc gcc gac gga cac ggc tgg ctg ccg 11664
Leu Arg His Glu Gly Asp Ala Ala Ala Asp Gly His Gly Trp Leu Pro
3875 3880 3885

ttc tcc tgg acc ggc gtc acg gtc gcc gcc tcc ggc gcc tcc acc ctg 11712
Phe Ser Trp Thr Gly Val Thr Val Ala Ala Ser Gly Ala Ser Thr Leu
3890 3895 3900

cac gtc cgt ctc acc gtc cgc acg gac gag gac gcg gtc gga ctg ctg 11760
His Val Arg Leu Thr Val Arg Thr Asp Glu Asp Ala Val Gly Leu Leu
3905 3910 3915 3920

gcc acc gac gca tcg gga cgc atc gtc atc tcc gcg ggg tcc ctc gcc 11808
Ala Thr Asp Ala Ser Gly Arg Ile Val Ile Ser Ala Gly Ser Leu Ala
3925 3930 3935

ttc cgg ccc gtc tcc gcc gag cag ctc cag gcc gcg cgc acc ggc tac 11856
Phe Arg Pro Val Ser Ala Glu Gln Leu Gln Ala Ala Arg Thr Gly Tyr
3940 3945 3950

cac gac cac ctc ttc cgc atc gaa tgg cgg ccg ctg cac ctc ccc acc 11904
His Asp His Leu Phe Arg Ile Glu Trp Arg Pro Leu His Leu Pro Thr
3955 3960 3965

aca ccg gca cgg aca gcc gac tgg gcc cta atc ggc ccc ggt gcc cgg 11952
Thr Pro Ala Arg Thr Ala Asp Trp Ala Leu Ile Gly Pro Gly Ala Arg
3970 3975 3980

cgg acg gcc gcc gtc ctg gag cgc aac ggc gcc tcc tgg cag gcc tac 12000
Arg Thr Ala Ala Val Leu Glu Arg Asn Gly Ala Ser Trp Gln Ala Tyr
3985 3990 3995 4000

ccg gac ccg gcg gct ctc gca gaa gcc ctg gcg gcc ggc gcc ccg gca 12048
Pro Asp Pro Ala Ala Leu Ala Glu Ala Leu Ala Ala Gly Ala Pro Ala

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4005 4010 4015

ccg ggc atg gtc gtc atc tcg tgc gag ccg gac ggc gca tcc gcc ccc 12096
Pro Gly Met Val Val Ile Ser Cys Glu Pro Asp Gly Ala Ser Ala Pro
4020 4025 4030

acc gat tcc gcc ctc acc gat tcc gcc ctc acc gat tcc gcc ccg gcc 12144
Thr Asp Ser Ala Leu Thr Asp Ser Ala Leu Thr Asp Ser Ala Pro Ala
4035 4040 4045

ggc tcg gcc ccg gcc gac tcc acc gcc ctc gcc gac gcc acc cgg caa 12192
Gly Ser Ala Pro Ala Asp Ser Thr Ala Leu Ala Asp Ala Thr Arg Gln
4050 4055 4060

gcc acc acc cgc gtc ctc gcc ctg ctc cag gaa tgg gtc gcc gac gaa 12240
Ala Thr Thr Arg Val Leu Ala Leu Leu Gln Glu Trp Val Ala Asp Glu
4065 4070 4075 4080

cgg ctc gcg gcc tgc cgc ctg gcc ctc ctc acg cac ggc tcg gtc acc 12288
Arg Leu Ala Ala Cys Arg Leu Ala Leu Leu Thr His Gly Ser Val Thr
4085 4090 4095

gcg acc ccc gac gag ccc gtg tcc gac ctc gca cac gcc gcc gtc tgg 12336
Ala Thr Pro Asp Glu Pro Val Ser Asp Leu Ala His Ala Ala Val Trp
4100 4105 4110

gga ctg gtc cgc tcc gtg cag acc gag aac ccc gac cgg ttc ctg ctg 12384
Gly Leu Val Arg Ser Val Gln Thr Glu Asn Pro Asp Arg Phe Leu Leu
4115 4120 4125

gcc gac acc gac gac acc gac gcc tcc cgc aac gcc ctt ccc ctg ctg 12432
Ala Asp Thr Asp Asp Thr Asp Ala Ser Arg Asn Ala Leu Pro Leu Leu
4130 4135 4140

gcc ggg gaa ccg cag atc gcc ctg cga aat ggt gcc gtc cgc atc ccg 12480
Ala Gly Glu Pro Gln Ile Ala Leu Arg Asn Gly Ala Val Arg Ile Pro
4145 4150 4155 4160

cgg atg aca cga gtg ccc gtc cgg cag cca cag ccg agc acc acc gac 12528
Arg Met Thr Arg Val Pro Val Arg Gln Pro Gln Pro Ser Thr Thr Asp
4165 4170 4175

gcc gac tgg gac ccg gag gcc acg gtc ctc atc acg ggc ggt acc ggc 12576
Ala Asp Trp Asp Pro Glu Ala Thr Val Leu Ile Thr Gly Gly Thr Gly
4180 4185 4190

gtc ctc ggc cgg ctc gtc gcc cgt cat ctc gcc acg gcc cac ggg gta 12624
Val Leu Gly Arg Leu Val Ala Arg His Leu Ala Thr Ala His Gly Val
4195 4200 4205

cgg cac ctg ctg ctg gcc acc cgc cgc ggc acg gcc gcg gac ggc gcc 12672
Arg His Leu Leu Leu Ala Thr Arg Arg Gly Thr Ala Ala Asp Gly Ala
4210 4215 4220

gcc gac ctg gtc gcc gaa ctc gcc ggc ctc ggc gcc gag gcc acg gtc 12720
Ala Asp Leu Val Ala Glu Leu Ala Gly Leu Gly Ala Glu Ala Thr Val
4225 4230 4235 4240

gcg gcc tgc gac atc ggg gac cgg gcg gcc gtc gcc gcg ctc ctc gac 12768
Ala Ala Cys Asp Ile Gly Asp Arg Ala Ala Val Ala Ala Leu Leu Asp
4245 4250 4255

caa gtg ccc gcg cag cac ccc ctg aaa gcc gtg atc cac acg gcc ggt 12816
Gln Val Pro Ala Gln His Pro Leu Lys Ala Val Ile His Thr Ala Gly
4260 4265 4270

gtg gtc gac gac ggc atc ctc acc tcg ctc act ccg gag cgc atg gag 12864
Val Val Asp Asp Gly Ile Leu Thr Ser Leu Thr Pro Glu Arg Met Glu
4275 4280 4285

gcc gtc ctg cac gcg aag gcg ttc ggc gcc gcg cac ctg cac gac ctg 12912
Ala Val Leu His Ala Lys Ala Phe Gly Ala Ala His Leu His Asp Leu
4290 4295 4300

acc cgc gac gcc ggc ctc acc acc ttc acc gtc ttc tcc tcg gcc gcc 12960
Thr Arg Asp Ala Gly Leu Thr Thr Phe Thr Val Phe Ser Ser Ala Ala

4305 4310 4315 4320

gcc tcc ttc ggc agt ccc gga cag ggc aac tac acc gcg gcg aac gcc 13008
Ala Ser Phe Gly Ser Pro Gly Gln Gly Asn Tyr Thr Ala Ala Asn Ala
4325 4330 4335

ttt ctg gac gcc ctg atg cag cac cgc cac acc cag gca ctg ccg ggc 13056
Phe Leu Asp Ala Leu Met Gln His Arg His Thr Gln Ala Leu Pro Gly
4340 4345 4350

cgg tcg ctc gcc tgg ggc ctt tgg ggc gag gcc gac ggc atg acc cgc 13104
Arg Ser Leu Ala Trp Gly Leu Trp Gly Glu Ala Asp Gly Met Thr Arg
4355 4360 4365

aac ctc gcc ggc acc gac ttc gcg cgc atg gcc cgc ggc ggc ctg ctc 13152
Asn Leu Ala Gly Thr Asp Phe Ala Arg Met Ala Arg Gly Gly Leu Leu
4370 4375 4380

ccc ctg tcc aac gca cag gga ctc gcg ctc ctc gac aca gcg gat cgc 13200
Pro Leu Ser Asn Ala Gln Gly Leu Ala Leu Leu Asp Thr Ala Asp Arg
4385 4390 4395 4400

ctc ggc cct ttc ggt gac ggg ctg ctc ctc gcc acc cgg ctc gac gcg 13248
Leu Gly Pro Phe Gly Asp Gly Leu Leu Leu Ala Thr Arg Leu Asp Ala
4405 4410 4415

gcc acc ctc cac gca cag gcc acg gcc ggc gcc ctg ccg cgc atc ctg 13296
Ala Thr Leu His Ala Gln Ala Thr Ala Gly Ala Leu Pro Arg Ile Leu
4420 4425 4430

cac ggg ctg atc cgc atc ccg gcc cgg cgg tcc gcc gac cac ggc atc 13344
His Gly Leu Ile Arg Ile Pro Ala Arg Arg Ser Ala Asp His Gly Ile
4435 4440 4445

gcg acc gac acc ccc gcc acg ctg cgc gag cgc ctg gcc gga ctc acc 13392
Ala Thr Asp Thr Pro Ala Thr Leu Arg Glu Arg Leu Ala Gly Leu Thr
4450 4455 4460

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atc ccc gcg cag cgc acc ggt ctc ctc ctg gaa ctc gta cgg acc cat 13440
Ile Pro Ala Gln Arg Thr Gly Leu Leu Leu Glu Leu Val Arg Thr His
4465 4470 4475 4480

gcc gcc gcc gtc ctc ggc cac ccc acc agc gcc gtc aca gcc gcg gac 13488
Ala Ala Ala Val Leu Gly His Pro Thr Ser Ala Val Thr Ala Ala Asp
4485 4490 4495

ggc gca ctc ccg gac gat ctg gtc ccg gcc gac acc gag ttc cgc gac 13536
Gly Ala Leu Pro Asp Asp Leu Val Pro Ala Asp Thr Glu Phe Arg Asp
4500 4505 4510

ctc ggc ttc gac tcg ctg acc gcc gtc gaa ctc cgc aac cgg atc aac 13584
Leu Gly Phe Asp Ser Leu Thr Ala Val Glu Leu Arg Asn Arg Ile Asn
4515 4520 4525

gcc gtc acc ggc ctg cgc ctc ccg gca acg ctc atc ttc gac cag ccc 13632
Ala Val Thr Gly Leu Arg Leu Pro Ala Thr Leu Ile Phe Asp Gln Pro
4530 4535 4540

agc ccc gcg gca ctc gcc gat cac ctc gcg acc cgc ctg acg gcc gag 13680
Ser Pro Ala Ala Leu Ala Asp His Leu Ala Thr Arg Leu Thr Ala Glu
4545 4550 4555 4560

gcg ggc acg ccg gac gag ccg gcc cct gcc gcc gcg gca gcc ggg gcc 13728
Ala Gly Thr Pro Asp Glu Pro Ala Pro Ala Ala Ala Ala Ala Gly Ala
4565 4570 4575

ggg agc gca ggg agt gcc gag acc gga cag cag cgc agt acg ggg agc 13776
Gly Ser Ala Gly Ser Ala Glu Thr Gly Gln Gln Arg Ser Thr Gly Ser
4580 4585 4590

gag aag cag cag acc agg ggc ggc acc tcc acc gaa acc gtc gaa tcc 13824
Glu Lys Gln Gln Thr Arg Gly Gly Thr Ser Thr Glu Thr Val Glu Ser
4595 4600 4605

ctg ttc tgg atc gga cac gac acc cgc cgc atc gag gag tcc atg gcc 13872
Leu Phe Trp Ile Gly His Asp Thr Arg Arg Ile Glu Glu Ser Met Ala

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4610 4615 4620

ctg ctc tcg gcg gcc tcc ttc ttc cgg ccc gcc ttc acg gac ccc tcg 13920
Leu Leu Ser Ala Ala Ser Phe Phe Arg Pro Ala Phe Thr Asp Pro Ser
4625 4630 4635 4640

gac atc ccg gag ccg acg ttc gtc cgg ctc gcc cag ggt gaa gcg cgc 13968
Asp Ile Pro Glu Pro Thr Phe Val Arg Leu Ala Gln Gly Glu Ala Arg
4645 4650 4655

gcc caa ggt gaa gca ctc gcc cgg ggc gaa aca cgg ccc gcc ctc atc 14016
Ala Gln Gly Glu Ala Leu Ala Arg Gly Glu Thr Arg Pro Ala Leu Ile
4660 4665 4670

tgc ctg ccc acc gtc gcc gcc gtg tcg agc gtg tac cag tac tca cgt 14064
Cys Leu Pro Thr Val Ala Ala Val Ser Ser Val Tyr Gln Tyr Ser Arg
4675 4680 4685

ttc gcg gcg gga ctg aac gga cac cga gac gtc tgg tac gtt cct gcg 14112
Phe Ala Ala Gly Leu Asn Gly His Arg Asp Val Trp Tyr Val Pro Ala
4690 4695 4700

cca ggg ttc ctg gag ggc gaa ccc ctg ccg tcc gga atc ggc gcg gtg 14160
Pro Gly Phe Leu Glu Gly Glu Pro Leu Pro Ser Gly Ile Gly Ala Val
4705 4710 4715 4720

acc cgc atg ttc gcc gac gcg atc gtc cgg ttc acc gac ggc gcg cct 14208
Thr Arg Met Phe Ala Asp Ala Ile Val Arg Phe Thr Asp Gly Ala Pro
4725 4730 4735

ttt gcg ctc gcc ggg cat tcc gcg ggc gga tgg ttc gtc tac gcg gtg 14256
Phe Ala Leu Ala Gly His Ser Ala Gly Gly Trp Phe Val Tyr Ala Val
4740 4745 4750

acg agt cat ctg gag cgt cta ggc gtc cgt ccg gaa gcg gtg gtg acc 14304
Thr Ser His Leu Glu Arg Leu Gly Val Arg Pro Glu Ala Val Val Thr
4755 4760 4765

atg gac gcc tat ctc ccg gac gac ggc atc gca cct gtc gcg tcc gcg 14352
Met Asp Ala Tyr Leu Pro Asp Asp Gly Ile Ala Pro Val Ala Ser Ala
4770 4775 4780

ctg aca agt gaa atc ttc gac cgc gtc acg cag ttt gtg gac gtg gac 14400
Leu Thr Ser Glu Ile Phe Asp Arg Val Thr Gln Phe Val Asp Val Asp
4785 4790 4795 4800

tac aca cgc ctg gtc gcc atg ggc gga tac ttc cgc atc ttc tcc ggc 14448
Tyr Thr Arg Leu Val Ala Met Gly Gly Tyr Phe Arg Ile Phe Ser Gly
4805 4810 4815

tgg agt cct ccg gac atc acc aca ccc gcc ctc ttc ctg cgc ggc cgg 14496
Trp Ser Pro Pro Asp Ile Thr Thr Pro Ala Leu Phe Leu Arg Gly Arg
4820 4825 4830

gac gga gaa cag atg ccg ccg ccg tgg gga gtt ccg cac acc gtt ctg 14544
Asp Gly Glu Gln Met Pro Pro Pro Trp Gly Val Pro His Thr Val Leu
4835 4840 4845

gac atc cag ggg aat cac ttc acg atg ctg gaa cag ttt gcg gat tcg 14592
Asp Ile Gln Gly Asn His Phe Thr Met Leu Glu Gln Phe Ala Asp Ser
4850 4855 4860

act gct cgg cat gtc gac gaa tgg ctg aca gaa atc gca tca gtg cgg 14640
Thr Ala Arg His Val Asp Glu Trp Leu Thr Glu Ile Ala Ser Val Arg
4865 4870 4875 4880

cgc tgatcgcgcc tctgatcgcg gtcctgatcg cggccctgat cggcgggtcg 14693
Arg

ggcacagccc ggtcggccgg tcggccagtc ggccagtcgg tggtatccgg tcggctccgg 14753

catcgatcag tgctttcccc cttacggcca tacgggcctt tctgagactt cttgaatttg 14813

ggagacagtg atg gac acg tcc agc gaa aag ctc gtc gac gcg ctt agg 14862
Met Asp Thr Ser Ser Glu Lys Leu Val Asp Ala Leu Arg
4885 4890

gcg tct ctg aag gcg aac cag acc ctg cgg gca cgt aat gag caa ctg 14910
Ala Ser Leu Lys Ala Asn Gln Thr Leu Arg Ala Arg Asn Glu Gln Leu
4895 4900 4905 4910
gca gcc gcc atg gag gcg tcc agc gag ccg att gcg att gtg ggg atg 14958
Ala Ala Ala Met Glu Ala Ser Ser Glu Pro Ile Ala Ile Val Gly Met
4915 4920 4925

gcg tgt cgt ttt ccg ggt ggg gtg tgt tcg ccg gag gag ttg tgg gag 15006
Ala Cys Arg Phe Pro Gly Gly Val Cys Ser Pro Glu Glu Leu Trp Glu
4930 4935 4940

ctg gtt gcg tcg ggt ggg gat gcg att ggt gaa ttt ccg gcc ggt cgg 15054
Leu Val Ala Ser Gly Gly Asp Ala Ile Gly Glu Phe Pro Ala Gly Arg
4945 4950 4955

ggg tgg gat ctg gag ggg ttg ttt gat tcg gac cct gac cgg tcg ggg 15102
Gly Trp Asp Leu Glu Gly Leu Phe Asp Ser Asp Pro Asp Arg Ser Gly
4960 4965 4970

acg tcg tac gcg cgg tat ggc ggg ttt ttg tat gag gcg ggg gag ttc 15150
Thr Ser Tyr Ala Arg Tyr Gly Gly Phe Leu Tyr Glu Ala Gly Glu Phe
4975 4980 4985 4990

gat gcg gac ttc ttc ggg atc agt ccg cgt gag gcg ttg gcg atg gat 15198
Asp Ala Asp Phe Phe Gly Ile Ser Pro Arg Glu Ala Leu Ala Met Asp
4995 5000 5005

ccg cag cag cgg ttg ttg ctg gag acg tcg tgg gag gcg ttc gag cgg 15246
Pro Gln Gln Arg Leu Leu Leu Glu Thr Ser Trp Glu Ala Phe Glu Arg
5010 5015 5020

gcg ggt atc gat ccg ctg tcg atg cgt ggc tcc cgt acg ggt gtc ttc 15294
Ala Gly Ile Asp Pro Leu Ser Met Arg Gly Ser Arg Thr Gly Val Phe
5025 5030 5035

gcc ggg gtg atg tac cac gac tac gga tcc cgc ctg ggt acc atc ccc 15342
Ala Gly Val Met Tyr His Asp Tyr Gly Ser Arg Leu Gly Thr Ile Pro

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5040 5045 5050

gag gga ttc gag ggc tac atc ggc aac ggt agc ggc ggc gcc gtc gcg 15390
Glu Gly Phe Glu Gly Tyr Ile Gly Asn Gly Ser Gly Gly Ala Val Ala
5055 5060 5065 5070

tcg ggc cgc gtc gcc tac acg ctc ggt ctc gag ggc cct gcc gtc tcg 15438
Ser Gly Arg Val Ala Tyr Thr Leu Gly Leu Glu Gly Pro Ala Val Ser
5075 5080 5085

gtg gac acg gca tgt tcg tcg tcg ttg gtg gcg ctg cat ctg gcg tgc 15486
Val Asp Thr Ala Cys Ser Ser Ser Leu Val Ala Leu His Leu Ala Cys
5090 5095 5100

cag tcg ctg cgg tcg ggt gag tgc acg ctc gcg ctg gcc ggc ggt gtg 15534
Gln Ser Leu Arg Ser Gly Glu Cys Thr Leu Ala Leu Ala Gly Gly Val
5105 5110 5115

acg gtg atg tcg acc ccg cac ctc ttc gtc gag ttc tca cgc cag cgc 15582
Thr Val Met Ser Thr Pro His Leu Phe Val Glu Phe Ser Arg Gln Arg
5120 5125 5130

gga ctg tcg gtg gac ggc cgc tgc aag tcc ttc gcg ggt gga gcc gac 15630
Gly Leu Ser Val Asp Gly Arg Cys Lys Ser Phe Ala Gly Gly Ala Asp
5135 5140 5145 5150

ggc acc ggc atg ggc gag ggc gtc ggg atg ctg ttg gtg gag cgg ttg 15678
Gly Thr Gly Met Gly Glu Gly Val Gly Met Leu Leu Val Glu Arg Leu
5155 5160 5165

tcg gat gcg gtg cgg ctg ggg cat cgg gtg ctg gcg gtg ctg cgc ggc 15726
Ser Asp Ala Val Arg Leu Gly His Arg Val Leu Ala Val Leu Arg Gly
5170 5175 5180

agt gcg gtc aat cag gac ggt gcg tcg aat ggg ttg acg gcg ccg aat 15774
Ser Ala Val Asn Gln Asp Gly Ala Ser Asn Gly Leu Thr Ala Pro Asn
5185 5190 5195

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ggt ccg gct cag gag cgg gtg atc cgg cag gcg ttg gcg aac gcg ggg 15822
Gly Pro Ala Gln Glu Arg Val Ile Arg Gln Ala Leu Ala Asn Ala Gly
5200 5205 5210

ttg tcc gtg gcg gat gtg gat gtg gtg gag ggg cat ggg acg ggc acg 15870
Leu Ser Val Ala Asp Val Asp Val Val Glu Gly His Gly Thr Gly Thr
5215 5220 5225 5230

acg ctg ggt gat ccg atc gag gcg cag gcg ttg ctc gcc acg tac ggg 15918
Thr Leu Gly Asp Pro Ile Glu Ala Gln Ala Leu Leu Ala Thr Tyr Gly
5235 5240 5245

cag cgg gcc ggt aac agg ccg ctg tgg ctg gga tcg gtg aag tcg aac 15966
Gln Arg Ala Gly Asn Arg Pro Leu Trp Leu Gly Ser Val Lys Ser Asn
5250 5255 5260

atc ggc cat gcg cag gct gcc gcg ggt gtg ggt ggg gtc atc aag atg 16014
Ile Gly His Ala Gln Ala Ala Ala Gly Val Gly Gly Val Ile Lys Met
5265 5270 5275

gtg atg gcg ttg cgg gag ggg gtg ttg ccg cgg acg ttg cat gtg gat 16062
Val Met Ala Leu Arg Glu Gly Val Leu Pro Arg Thr Leu His Val Asp
5280 5285 5290

gag ccg tcg ccg cag gtg gac tgg tcc gcg ggg gcg gtg cgg ctg ctg 16110
Glu Pro Ser Pro Gln Val Asp Trp Ser Ala Gly Ala Val Arg Leu Leu
5295 5300 5305 5310

acg gag gcg gtg ccg tgg ccg ggg gac gcg gca ggg cgg ttg cgg cgg 16158
Thr Glu Ala Val Pro Trp Pro Gly Asp Ala Ala Gly Arg Leu Arg Arg
5315 5320 5325

gcg gga gtg tcg tcg ttc ggg gtc agt ggc acg aat gcg cat gtg att 16206
Ala Gly Val Ser Ser Phe Gly Val Ser Gly Thr Asn Ala His Val Ile
5330 5335 5340

ttg gag gag gcg ccg gcg gcg ggg ggc tgt gtt gcc ggg ggt ggg gtg 16254
Leu Glu Glu Ala Pro Ala Ala Gly Gly Cys Val Ala Gly Gly Gly Val

5345 5350 5355

ttg gag ggt gct ccg ggt ctt gcc att tcg gtg gct gag tcg gtg gcc 16302
Leu Glu Gly Ala Pro Gly Leu Ala Ile Ser Val Ala Glu Ser Val Ala
5360 5365 5370

gct cca gtg gct gtg tct gcg ccg gtg gct gag tcg gtg ccg gtg ccg 16350
Ala Pro Val Ala Val Ser Ala Pro Val Ala Glu Ser Val Pro Val Pro
5375 5380 5385 5390

gtg ccg gtg ccg gtt cct gtg ccg gtg tcg gct agg tct gag gct ggg 16398
Val Pro Val Pro Val Pro Val Pro Val Ser Ala Arg Ser Glu Ala Gly
5395 5400 5405

ttg cgg gcg cag gcg gag gcg ttg cgt cag tac gtg gca gtc cgg ccg 16446
Leu Arg Ala Gln Ala Glu Ala Leu Arg Gln Tyr Val Ala Val Arg Pro
5410 5415 5420

gac gtt tcg ctt gcc gat gtg ggt gcg ggt ctg gcc tgt ggg cgg gct 16494
Asp Val Ser Leu Ala Asp Val Gly Ala Gly Leu Ala Cys Gly Arg Ala
5425 5430 5435

gtg ctg gag cat cgt gcg gtc gtc ctg gcc gcg gac cgt gag gag ctg 16542
Val Leu Glu His Arg Ala Val Val Leu Ala Ala Asp Arg Glu Glu Leu
5440 5445 5450

gtg caa ggg ttg ggg gcg ctg gcg gcg ggt gag ccg gat cgg cgg gtg 16590
Val Gln Gly Leu Gly Ala Leu Ala Ala Gly Glu Pro Asp Arg Arg Val
5455 5460 5465 5470

acc acg ggt cat gcg ccg ggt ggt gac cgg ggc ggt gtc gtc ttc gtg 16638
Thr Thr Gly His Ala Pro Gly Gly Asp Arg Gly Gly Val Val Phe Val
5475 5480 5485

ttt ccc gga cag ggt ggg cag tgg gcc ggg atg ggt gtg cgt ctg ctc 16686
Phe Pro Gly Gln Gly Gly Gln Trp Ala Gly Met Gly Val Arg Leu Leu
5490 5495 5500

gcc tcc tct ccg gtg ttc gcc cgg cgg atg cag gcg tgc gag gag gct 16734
Ala Ser Ser Pro Val Phe Ala Arg Arg Met Gln Ala Cys Glu Glu Ala
5505 5510 5515

ctg gcg ccg tgg gtg gac tgg tct gtg gtg gac atc ctg cgc cgg gac 16782
Leu Ala Pro Trp Val Asp Trp Ser Val Val Asp Ile Leu Arg Arg Asp
5520 5525 5530

gcg ggg gat gcg gtg tgg gag cgg gcc gat gtg gtc cag cct gtg ctg 16830
Ala Gly Asp Ala Val Trp Glu Arg Ala Asp Val Val Gln Pro Val Leu
5535 5540 5545 5550

ttc agc gtc atg gtg tct ttg gct gct ctg tgg cgt tcc tac ggt atc 16878
Phe Ser Val Met Val Ser Leu Ala Ala Leu Trp Arg Ser Tyr Gly Ile
5555 5560 5565

gaa ccc gac gcg gtc ctt ggc cat tcc cag ggc gag atc gcg gcc gcg 16926
Glu Pro Asp Ala Val Leu Gly His Ser Gln Gly Glu Ile Ala Ala Ala
5570 5575 5580

cat gtg tgt ggg gcg ctg agc ctg aag gac gcg gcg aag act gtt gcg 16974
His Val Cys Gly Ala Leu Ser Leu Lys Asp Ala Ala Lys Thr Val Ala
5585 5590 5595

ctg cgc agc cgg gcg ctg gcc gct gtg cgg ggc cgg ggc ggc atg gcc 17022
Leu Arg Ser Arg Ala Leu Ala Ala Val Arg Gly Arg Gly Gly Met Ala
5600 5605 5610

tca gtg ccg ctg cct gcc cag gag gtg gag cag ctc att ggt gag cgg 17070
Ser Val Pro Leu Pro Ala Gln Glu Val Glu Gln Leu Ile Gly Glu Arg
5615 5620 5625 5630

tgg gcg ggg cgg ttg tgg gtg gcg gcg gtc aac ggc ccc cgc tcc acc 17118
Trp Ala Gly Arg Leu Trp Val Ala Ala Val Asn Gly Pro Arg Ser Thr
5635 5640 5645

gcc gtc tcg ggg gat gcc gag gcg gtg gac gag gtg ctg gcg tac tgt 17166
Ala Val Ser Gly Asp Ala Glu Ala Val Asp Glu Val Leu Ala Tyr Cys

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5650 5655 5660

gcc ggc acc ggg gtg cgg gcc cgg cgg atc ccg gtc gac tat gcc tcg 17214
Ala Gly Thr Gly Val Arg Ala Arg Arg Ile Pro Val Asp Tyr Ala Ser
5665 5670 5675

cac tgc ccc cat gtg cag ccc ctg cgg gag gag ttg ctg gag ctg ctg 17262
His Cys Pro His Val Gln Pro Leu Arg Glu Glu Leu Leu Glu Leu Leu
5680 5685 5690

ggg gac atc agc ccg cag ccg tcc ggc gtg ccg ttc ttc tcc acg gtg 17310
Gly Asp Ile Ser Pro Gln Pro Ser Gly Val Pro Phe Phe Ser Thr Val
5695 5700 5705 5710

gag ggc acc tgg ctg gac acc aca acc ctg gac gcc gcc tac tgg tac 17358
Glu Gly Thr Trp Leu Asp Thr Thr Thr Leu Asp Ala Ala Tyr Trp Tyr
5715 5720 5725

cgc aac ctg cac cag cct gtc cgt ttc agc gat gcc gtc cag gcc ctg 17406
Arg Asn Leu His Gln Pro Val Arg Phe Ser Asp Ala Val Gln Ala Leu
5730 5735 5740

gcg gat gac gga cac cgc gtc ttc gtc gaa gtc agc ccc cac ccc acc 17454
Ala Asp Asp Gly His Arg Val Phe Val Glu Val Ser Pro His Pro Thr
5745 5750 5755

ctc gtc ccc gcc atc gaa gac acc acc gaa gac acc gcc gaa gac gtc 17502
Leu Val Pro Ala Ile Glu Asp Thr Thr Glu Asp Thr Ala Glu Asp Val
5760 5765 5770

acc gcg atc ggc agc ctc cgc cgc ggc gac aac gac acc cgc cgc ttc 17550
Thr Ala Ile Gly Ser Leu Arg Arg Gly Asp Asn Asp Thr Arg Arg Phe
5775 5780 5785 5790

ctc acc gcc ctc gcc cac acc cac acc acc ggc atc ggc aca ccc acc 17598
Leu Thr Ala Leu Ala His Thr His Thr Thr Gly Ile Gly Thr Pro Thr
5795 5800 5805

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acc tgg cac cac cac tac acc cac cac cac acc cac ccc cac aac cac   17646
Thr Trp His His His Tyr Thr His His His Thr His Pro His Asn His
            5810                5815                5820

cac ctc gac ctc ccc act tat ccc ttc caa cgc cag cac tac tgg ctc   17694
His Leu Asp Leu Pro Thr Tyr Pro Phe Gln Arg Gln His Tyr Trp Leu
        5825                5830                5835

gac gct ccc acg gga gca ggt gac gtc gcc gct gct ggc ttg gag ccg   17742
Asp Ala Pro Thr Gly Ala Gly Asp Val Ala Ala Ala Gly Leu Glu Pro
    5840                5845                5850

gcc gaa cac cct ctg ctc gcg gca aca gtc caa ctc gca gac acg gac   17790
Ala Glu His Pro Leu Leu Ala Ala Thr Val Gln Leu Ala Asp Thr Asp
5855                5860                5865                5870

ggc tgc cta ctg acg ggt cgc ctg tcc ttg cgc tcg cat ccg tgg ctg   17838
Gly Cys Leu Leu Thr Gly Arg Leu Ser Leu Arg Ser His Pro Trp Leu
                5875                5880                5885

ggc gat tac gag gtg ggg ggt gcg gtc ctg ctg tcg ggg tcg gcg ttc   17886
Gly Asp Tyr Glu Val Gly Gly Ala Val Leu Leu Ser Gly Ser Ala Phe
            5890                5895                5900

gtg gag ctg gcg gtc cag gtt ggc gaa cgc gtg ggc tgc acc cga atc   17934
Val Glu Leu Ala Val Gln Val Gly Glu Arg Val Gly Cys Thr Arg Ile
        5905                5910                5915

gag caa ctc act gtg cat gcg ccg ctg gtg gtt cct gtg ggt ggg ggt   17982
Glu Gln Leu Thr Val His Ala Pro Leu Val Val Pro Val Gly Gly Gly
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Val Ser Val Gln Val Gly Val Ala Ala Ala Asp Gly Glu Gly Arg Arg
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Leu Val Ser Val Tyr Ala Arg Gly Gly Ser Ala Cys Gly Gly Gly Gly
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Val Arg Val Trp Ala Val Gly Arg Gly Gly Gly Arg Glu Ala Val Ser
6115 6120 6125

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Val Val Val Gly Asp Glu Ala Gly Val Pro Val Ala Ser Val Asp Arg
6130 6135 6140

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6255 6260 6265 6270

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Asp Leu Asp Thr Asp Thr Asp Thr Gly Thr Asp Leu Asp Thr Gly Ala
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Ser His Ile Ala Thr Val Leu Gly His Thr Thr Pro Asp Thr Ile Pro
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Glu Leu Arg Asn Arg Leu Ser Arg Thr Thr Gly Leu Arg Leu Pro Thr
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Glu Arg Leu Ser Asp Ala Arg Arg Asn Gly His Arg Val Leu Ala Val
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7040 7045 7050

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Val Ile Lys Met Val Met Ala Leu Arg Asn Gly Leu Leu Pro Arg Thr
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Tyr Thr Leu Ala His Ala Arg Ala Val Phe Asp His Arg Ala Thr Leu
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Thr His His Ile Thr Ala His Glu Asn Asp Leu Ala Ile Ala Ala Ile
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Pro Thr Asn His Ala Phe His Ser Pro His Thr Asn Pro Ile Leu Asn
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Ser Val Ser Ala Gly Arg Arg Gly Ser Leu Tyr Ala Val Gln Trp Ala
7970 7975 7980

gag gtg ggt cct gtg ccg gtg tgt ggg cag gcg tgg gcg tgg cac gag 24174
Glu Val Gly Pro Val Pro Val Cys Gly Gln Ala Trp Ala Trp His Glu
7985 7990 7995

gac gtg ggt gag agc ggt ggt ggg cct gtg ccg ggg gtg gtg gtg ttg 24222
Asp Val Gly Glu Ser Gly Gly Gly Pro Val Pro Gly Val Val Val Leu
8000 8005 8010

cgg tgc ccg gat gcc ggt gcc gat ggc ggc ggt ggc ggt ggt gtg ggt 24270
Arg Cys Pro Asp Ala Gly Ala Asp Gly Gly Gly Gly Gly Gly Val Gly
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Glu Val Val Gly Gly Val Leu Gly Val Val Gln Gly Trp Leu Gly Leu
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Glu Arg Phe Ala Gly Ser Arg Leu Val Val Val Thr Arg Gly Ala Val
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Val Ala Gly Pro Glu Asp Gly Pro Val Asp Val Val Gly Ala Ala Val
8065 8070 8075

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Trp Gly Leu Val Arg Ser Ala Gln Ala Glu His Pro Asp Arg Phe Val

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Leu Leu Asp Leu Asp Thr Asp Leu Asp Ser Gly Ala Asp Ala Asp Ala
8095 8100 8105 8110

ggc aac gag gcc ggt atg ggg tct ggt ctg gat ggt ggg cgt gtg gct 24558
Gly Asn Glu Ala Gly Met Gly Ser Gly Leu Asp Gly Gly Arg Val Ala
8115 8120 8125

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Ala Val Val Ala Cys Gly Glu Pro Gln Leu Ala Val Arg Gly Glu Arg
8130 8135 8140

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Val Leu Ala Ala Arg Leu Thr Arg Leu Glu Ser Pro Val Asp Val Ser
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8160 8165 8170

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8175 8180 8185 8190

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Val Cys Gly Val Arg Asp Leu Leu Leu Val Ser Arg Arg Gly Pro Asp
8195 8200 8205

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Glu Val Arg Ile Val Ala Cys Asp Val Gly Glu Arg Arg Glu Val Val
8225 8230 8235

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8240 8245 8250

cat gcg gct ggt gtg ctg gac gat gcg acg atc gcc tct ctc acg ccc 24990
His Ala Ala Gly Val Leu Asp Asp Ala Thr Ile Ala Ser Leu Thr Pro
8255 8260 8265 8270

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Glu Arg Leu Gly Thr Val Phe Ala Ala Lys Val Asp Ala Ala Leu Leu
8275 8280 8285

ctg gat gag ctg acg cgg ggt atg gag ctg tcg gcg ttc gtg ctg ttc 25086
Leu Asp Glu Leu Thr Arg Gly Met Glu Leu Ser Ala Phe Val Leu Phe
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Ser Ser Ala Ala Gly Ile Leu Gly Ser Ala Gly Gln Gly Asn Tyr Ala
8305 8310 8315

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Ala Ala Asn Ala Ala Leu Asp Ala Leu Ala Tyr Arg Arg Arg Ala Ala
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8335 8340 8345 8350

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Gly Met Thr Gly His Leu Ala Gly Thr Asp His Arg Arg Ile Ile Arg
8355 8360 8365

tcc ggt ctg cat ccc atg tcg acc ccg gac gca ctg gct ctc ttc gat 25326
Ser Gly Leu His Pro Met Ser Thr Pro Asp Ala Leu Ala Leu Phe Asp
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8385 8390 8395

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Pro Ala Pro Pro Leu Pro Pro Leu Leu Gln Asp Leu Leu Pro Ala Thr
8400 8405 8410

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Arg Arg Arg Thr Thr Arg Thr Thr Thr Thr Gly Gly Ala Asp Asn Gly
8415 8420 8425 8430

gcc cag ctg cat gcc cgg ctg gcc ggc cag aca cac gaa caa cag cac 25518
Ala Gln Leu His Ala Arg Leu Ala Gly Gln Thr His Glu Gln Gln His
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acc acc ctc ctc gcc ctg gtc cgc tcc cac atc gcc acc gtc ctc ggc 25566
Thr Thr Leu Leu Ala Leu Val Arg Ser His Ile Ala Thr Val Leu Gly
8450 8455 8460

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His Asn Ala Pro Glu Met Ile Pro Val Asp Ser Ala Phe Arg Asp Leu
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Gly Phe Asp Ser Leu Thr Ala Val Glu Leu Arg Asn Arg Leu Gly Glu
8480 8485 8490

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8495 8500 8505 8510

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Ala Glu Gly Glu Thr Pro Ser Gln Val Ala Leu His Gln Val Ala Ala
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Asp Glu Pro Ile Ala Ile Val Gly Met Ala Cys Arg Phe Pro Gly Gly
8545 8550 8555

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Val Cys Ser Pro Glu Glu Leu Trp Glu Leu Val Ala Ser Gly Gly Asp
8560 8565 8570

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Phe Asp Ser Asp Pro Asp Arg Ser Gly Thr Ser Tyr Ala Arg Tyr Gly
8595 8600 8605

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Gly Phe Leu Tyr Glu Ala Gly Glu Phe Asp Ala Asp Phe Phe Gly Ile
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Ser Pro Arg Glu Ala Leu Ala Met Asp Pro Gln Gln Arg Leu Leu Leu
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Glu Thr Ser Trp Glu Ala Phe Glu Arg Ala Gly Ile Asp Pro Leu Ser
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Met Arg Gly Ser Arg Thr Gly Val Phe Ala Gly Val Met Tyr His Asp
8655 8660 8665 8670

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Tyr Ala Ala Arg Leu His His Val Pro Glu Gly Phe Glu Gly Leu Ile
8675 8680 8685

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Phe Gly Leu Glu Gly Pro Ala Val Thr Val Asp Thr Ala Cys Ser Ser
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tcg ttg gtg gcg ttg cat tgg gcg gcg cag gcg ttg cgt gcg ggt gag 26382
Ser Leu Val Ala Leu His Trp Ala Ala Gln Ala Leu Arg Ala Gly Glu
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Cys Ser Met Ala Leu Ala Gly Gly Val Thr Val Met Ser Ser Pro Gly
8735 8740 8745 8750

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Thr Phe Val Glu Phe Ser Arg Gln Arg Gly Leu Ala Ala Asp Gly Arg
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Cys Lys Ala Tyr Ser Ala Ala Ala Asp Gly Thr Gly Trp Ala Glu Gly
8770 8775 8780

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Val Gly Met Leu Leu Val Glu Arg Leu Ser Asp Ala Arg Arg Asn Gly
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His Arg Val Leu Ala Val Val Arg Gly Ser Ala Val Asn Gln Asp Gly
8800 8805 8810

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Ala Ser Asn Gly Leu Thr Ala Pro Asn Gly Pro Ser Gln Gln Arg Val
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Ile Arg Gln Ala Leu Ala Asn Ala Gly Leu Thr Pro Ala Asp Val Asp
8835 8840 8845

gca gtg gag ggc cac ggc acc ggg acc act ctg ggg gac ccg atc gag 26766
Ala Val Glu Gly His Gly Thr Gly Thr Thr Leu Gly Asp Pro Ile Glu
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Ala Gln Ala Leu Leu Ala Ala Tyr Gly Gln His Arg Pro His His Arg
8865 8870 8875

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Pro Leu Trp Leu Gly Ser Leu Lys Ser Asn Ile Gly His Ala Gln Ala
8880 8885 8890

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Ala Ala Gly Val Gly Gly Val Ile Lys Met Val Met Ala Leu Arg Asn
8895 8900 8905 8910

ggg ctg ctg cca cag acc ctc cac gtg gac gag ccc acc ccc cag gtc 26958
Gly Leu Leu Pro Gln Thr Leu His Val Asp Glu Pro Thr Pro Gln Val
8915 8920 8925

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Asp Trp Ser Thr Gly Ala Val Gln Leu Leu Thr Gln Pro Val Pro Trp
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ccc gcc gac ccg gcc ggc cgg cca cgc cac gcc ggc gtg tca tca ttc 27054
Pro Ala Asp Pro Ala Gly Arg Pro Arg His Ala Gly Val Ser Ser Phe
8945 8950 8955

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Gly Val Ser Gly Thr Asn Ala His Val Ile Leu Glu Glu Ala Pro Ala
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Ala Ala Gly Gly Ala Ala Gly Gly Gly Val Ser Val Gly Ala Pro Asn
8975 8980 8985 8990

cca gcc ctt ccg gtg gct gag tct gag ccg gtg ccg gtg ccg gtg ccg 27198
Pro Ala Leu Pro Val Ala Glu Ser Glu Pro Val Pro Val Pro Val Pro

8995 9000 9005

gtg tcg gcg agg tct gag gcc ggg ttg cgg gcg cag gca cag gcg ttg 27246
Val Ser Ala Arg Ser Glu Ala Gly Leu Arg Ala Gln Ala Gln Ala Leu
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Arg Gln Tyr Val Ala Ala Arg Pro Asp Met Ser Pro Ala Asp Ile Gly
9025 9030 9035

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Ala Gly Leu Ala Arg Gly Arg Ala Val Leu Glu His Arg Ala Val Ile
9040 9045 9050

ctg gcc gcg gac cgc gag gaa ctg gcg cag gca ctg aca gcc ctg gca 27390
Leu Ala Ala Asp Arg Glu Glu Leu Ala Gln Ala Leu Thr Ala Leu Ala
9055 9060 9065 9070

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Ala Gly Glu Pro His Pro His Ile Thr Thr Gly His Thr Arg Gly Ser
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Asp Arg Gly Gly Val Val Phe Val Phe Pro Gly Gln Gly Gly Gln Trp
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Ala Gly Met Gly Leu Thr Leu Leu Thr Ser Ser Pro Val Phe Ala Glu
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His Ile Asp Ala Cys Glu Lys Ala Leu Thr Pro Trp Val Pro Trp Ser
9120 9125 9130

ctg acc gac atc ctg cac cgc gac ccc gac gac ccc gca tgg caa caa 27630
Leu Thr Asp Ile Leu His Arg Asp Pro Asp Asp Pro Ala Trp Gln Gln
9135 9140 9145 9150

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gcc gac gtg gtc cag ccc gtg ctc ttc agc atc atg gtc tcc ctc gcc 27678
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9155 9160 9165

gcc ctg tgg cgc tcc tac ggc atc gaa ccc gac gcg gtc ctc ggc cac 27726
Ala Leu Trp Arg Ser Tyr Gly Ile Glu Pro Asp Ala Val Leu Gly His
9170 9175 9180

tcc cag gga gaa atc gcc gcc gcc cac atc tgc ggc gca ctc agc ctg 27774
Ser Gln Gly Glu Ile Ala Ala Ala His Ile Cys Gly Ala Leu Ser Leu
9185 9190 9195

aaa gac gcc gcc aaa acc gtt gca ctg cgc agc cag gca ctg gcc gcc 27822
Lys Asp Ala Ala Lys Thr Val Ala Leu Arg Ser Gln Ala Leu Ala Ala
9200 9205 9210

gta cga ggc cgg ggc gcc atg gtc tca ctg ccc ctg ccc gcc cag gac 27870
Val Arg Gly Arg Gly Ala Met Val Ser Leu Pro Leu Pro Ala Gln Asp
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Val Gln Gln Leu Ile Ser Glu Arg Trp Glu Gly Gln Leu Trp Val Ala
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gcc ctc aac ggc ccc cac tcc acc acc gtc tcc ggc gac acc acc gca 27966
Ala Leu Asn Gly Pro His Ser Thr Thr Val Ser Gly Asp Thr Thr Ala
9250 9255 9260

gta gaa gaa ctc ctc acc cac tgt gcc gac acc ggc cta cgg gcc aaa 28014
Val Glu Glu Leu Leu Thr His Cys Ala Asp Thr Gly Leu Arg Ala Lys
9265 9270 9275

cgc atc ccc gtc gac tac gcc tcc cac tgc ccc cac gtc caa ccc ctc 28062
Arg Ile Pro Val Asp Tyr Ala Ser His Cys Pro His Val Gln Pro Leu
9280 9285 9290

cac gac gaa ctc ctg cac ctg ctg gga gac atc acc ccc cag ccg tcc 28110
His Asp Glu Leu Leu His Leu Leu Gly Asp Ile Thr Pro Gln Pro Ser

9295 9300 9305 9310

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Thr Met Pro Phe Phe Ser Thr Val Val Gly His Leu Val Trp Tyr Thr
9315 9320 9325

aca acc ctg gac gcc gcc tac tgg tac cgc aac ctc cac cag ccc gtc 28206
Thr Thr Leu Asp Ala Ala Tyr Trp Tyr Arg Asn Leu His Gln Pro Val
9330 9335 9340

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Arg Phe Ser His Ala Ile Gln Thr Leu Thr Asp Asp Gly His Arg Pro
9345 9350 9355

ttc atc gaa atc agt ccc cac ccc acc ctc gtc ccc gcc atc gaa gac 28302
Phe Ile Glu Ile Ser Pro His Pro Thr Leu Val Pro Ala Ile Glu Asp
9360 9365 9370

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Thr Thr Glu Asn Thr Thr Glu Asn Ile Thr Ala Thr Gly Ser Leu Arg
9375 9380 9385 9390

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Arg Gly Asp Asn Asp Thr His Arg Phe Leu Thr Ala Leu Ala His Thr
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His Thr Thr Gly Ile Arg Thr Pro Thr Thr Trp His His His Tyr Thr
9410 9415 9420

caa acc cac ccc cac ccc cac aac cac cac ctc gac ctg ccc acc tac 28494
Gln Thr His Pro His Pro His Asn His His Leu Asp Leu Pro Thr Tyr
9425 9430 9435

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Pro Phe Gln His Gln His Tyr Trp Leu Gln Pro Pro Thr Thr Thr Thr
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gac ctc acc acc acc ggc ctc acc ccc acc cac cac ccc ctc ctc acc 28590
Asp Leu Thr Thr Thr Gly Leu Thr Pro Thr His His Pro Leu Leu Thr
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Ala Thr Leu Thr Leu Ala Asn Asn Asn Thr Gln Leu Leu Thr Gly Arg
9475 9480 9485

ctc tcc cta cgc acc cac ccc tgg ctc acc gac cac acc gtc gtc ggt 28686
Leu Ser Leu Arg Thr His Pro Trp Leu Thr Asp His Thr Val Val Gly
9490 9495 9500

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Thr Thr Leu Val Pro Gly Thr Ala Leu Leu Glu Leu Ala Leu Gln Ala
9505 9510 9515

acc acg acc gac cac ctc gaa gaa ctc gcc ctc cac acg cct ctc gtc 28782
Thr Thr Thr Asp His Leu Glu Glu Leu Ala Leu His Thr Pro Leu Val
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Ile Pro Arg Glu Gly Ala Val Asp Val Gln Val His Ile Asn Pro Pro
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acc aag acc tcg cgc att gag aca ggc cgt agc cac gat gat ctg tcg 28974
Thr Lys Thr Ser Arg Ile Glu Thr Gly Arg Ser His Asp Asp Leu Ser
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Met Trp Pro Pro Ala Gly Ala Val Arg Cys Ala Asp Glu Glu Leu Ala

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9600 9605 9610

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Phe Arg Gly Leu Thr Ala Ala Trp Arg Leu Gly Asp Glu Val Phe Ala
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Leu His Pro Ala Leu Leu Asp Ala Ala Leu His Ala Ala Ala Phe Ala
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Pro Ser Gly Ser Leu Pro Gln Gly Ser Val Pro Phe Ser Phe Thr Gly
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Pro Ala Asp Pro Asn Ser Gly His Ala Ala Val Ser Val Leu Val Thr
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9745 9750 9755

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Val Val Ala Gly Pro Glu Asp Gly Pro Val Asp Gly Pro Val Asp Val
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ctg acg ggt gtc gtg cat gcg gct ggt gtg ctg gac gat gcg acg atc 30366
Leu Thr Gly Val Val His Ala Ala Gly Val Leu Asp Asp Ala Thr Ile
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Ala Ser Leu Thr Pro Glu Arg Leu Gly Thr Val Phe Ala Ala Lys Val
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His Glu Gln Gln His Thr Thr Leu Leu Ala Leu Val Arg Ser His Ile
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<212> PRT
<213> Streptomyces avermitilis

<400> 3
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Val Leu Gly Val Ala Asp Glu Ala Asp Gly Gly Val Val Phe Val Phe
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Pro Gly Gln Gly Pro Gln Trp Pro Gly Met Gly Arg Glu Leu Leu Asp
35 40 45

Ala Ser Asp Val Phe Arg Glu Ser Val Arg Ala Cys Glu Ala Ala Phe
50 55 60

Ala Pro Tyr Val Asp Trp Ser Val Glu Gln Val Leu Arg Asp Ser Pro
65 70 75 80

Asp Ala Pro Gly Leu Asp Arg Val Asp Val Val Gln Pro Thr Leu Phe
85 90 95

Ala Val Met Ile Ser Leu Ala Ala Leu Trp Arg Ser Gln Gly Val Glu

100 105 110

Pro Cys Ala Val Leu Gly His Ser Leu Gly Glu Ile Ala Ala Ala His
115 120 125

Val Ser Gly Gly Leu Ser Leu Ala Asp Ala Ala Arg Val Val Thr Leu
130 135 140

Trp Ser Gln Ala Gln Thr Thr Leu Ala Gly Thr Gly Ala Leu Val Ser
145 150 155 160

Val Ala Ala Thr Pro Asp Glu Leu Leu Pro Arg Ile Ala Pro Trp Thr
165 170 175

Glu Asp Asn Pro Ala Arg Leu Ala Val Ala Ala Val Asn Gly Pro Arg
180 185 190

Ser Thr Val Val Ser Gly Ala Arg Glu Ala Val Ala Asp Leu Val Ala
195 200 205

Asp Leu Thr Ala Ala Gln Val Arg Thr Arg Met Ile Pro Val Asp Val
210 215 220

Pro Ala His Ser Pro Leu Met Tyr Ala Ile Glu Glu Arg Val Val Ser
225 230 235 240

Gly Leu Leu Pro Ile Thr Pro Arg Pro Ser Arg Ile Pro Phe His Ser
245 250 255

Ser Val Thr Gly Gly Arg Leu Asp Thr Arg Glu Leu Asp Ala Ala Tyr
260 265 270

Trp Tyr Arg Asn Met Ser Ser Thr Val Arg Phe Glu Pro Ala Ala Arg
275 280 285

Leu Leu Leu Gln Gln Gly Pro Lys Thr Phe Val Glu Met Ser Pro His
290 295 300

Pro Val Leu Thr Met Gly Leu Gln Glu Leu Ala Pro Asp Leu Gly Asp
305 310 315 320

Thr Thr Gly Thr Ala Asp Thr Val Ile Met Gly Thr Leu Arg Arg Gly
325 330 335

Gln Gly Thr Leu Asp His Phe Leu Thr Ser Leu Ala Gln Leu Arg Gly
340 345 350

His Gly Glu Thr Ser Ala Thr Thr Val Leu Ser Ala Arg Leu Thr Ala
355 360 365

Leu Ser Pro Thr Gln Gln Gln Ser Leu Leu Leu Asp Leu Val Arg Ala
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His Thr Met Ala Val Leu Asn Asp Asp Gly Asn Glu Arg Thr Ala Ser
385 390 395 400

Asp Ala Gly Pro Ser Ala Ser Phe Ala His Leu Gly Phe Asp Ser Val
405 410 415

Met Gly Val Glu Leu Arg Asn Arg Leu Ser Lys Ala Thr Gly Leu Arg
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Leu Pro Val Thr Leu Ile Phe Asp His Thr Thr Pro Ala Ala Val Ala
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Ala Arg Leu Arg Thr Ala Ala Leu Gly His Leu Asp Glu Asp Thr Ala
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Pro Val Pro Asp Ser Pro Ser Gly His Gly Gly Thr Ala Ala Ala Asp
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Arg Ser Pro Lys Asp Leu Trp Glu Leu Ala Ala Ser Gly Gly Asp Ala
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Ile Gly Pro Phe Pro Thr Asp Arg Gly Trp Pro Thr Glu Gln Arg His
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Ala Gln Asp Pro Thr Gln Pro Gly Thr Phe Tyr Pro Gln Gly Gly Gly
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Phe Leu His Asp Ala Ala His Phe Asp Ala Gly Phe Phe Gly Ile Ser
545 550 555 560

Pro Arg Glu Ala Leu Ala Met Asp Pro Gln Gln Arg Leu Leu Leu Glu
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Thr Ser Trp Glu Ala Phe Glu Arg Ala Gly Ile Asp Pro Leu Ser Val
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Arg Gly Ser Arg Thr Gly Val Phe Ala Gly Ala Leu Ser Phe Asp Tyr
595 600 605

Gly Pro Arg Met Asp Thr Ala Ser Ser Glu Gly Ala Ala Asp Val Glu
610 615 620

Gly His Ile Leu Thr Gly Thr Thr Gly Ser Val Leu Ser Gly Arg Ile
625 630 635 640

Ala Tyr Ser Phe Gly Leu Glu Gly Pro Ala Ile Thr Val Asp Thr Gly
645 650 655

Cys Ser Ala Ser Leu Val Thr Leu His Leu Ala Cys Gln Ser Leu Arg
660 665 670

Ser Gly Glu Cys Thr Leu Ala Leu Ala Gly Gly Val Ser Val Met Ser
675 680 685

Thr Leu Gly Met Phe Ile Glu Phe Ser Arg Gln Arg Gly Leu Ser Val
690 695 700

Asp Gly Arg Cys Lys Ala Tyr Ser Ala Ala Ala Asp Gly Thr Gly Trp

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Entered 05/21/2004

705 710 715 720

Gly Glu Gly Val Gly Met Leu Leu Val Glu Arg Leu Ser Asp Ala Val
725 730 735

Arg Leu Gly His Arg Val Leu Ala Val Val Arg Gly Ser Ala Val Asn
740 745 750

Gln Asp Gly Ala Ser Asn Gly Leu Thr Ala Pro Asn Gly Pro Ala Gln
755 760 765

Glu Arg Val Ile Arg Gln Ala Leu Ala Asn Ala Gly Leu Ser Val Ala
770 775 780

Asp Val Asp Val Val Glu Gly His Gly Thr Gly Thr Thr Leu Gly Asp
785 790 795 800

Pro Ile Glu Ala Gln Ala Leu Leu Ala Thr Tyr Gly Gln Arg Ala Gly
805 810 815

Asp Arg Pro Leu Trp Leu Gly Ser Leu Lys Ser Asn Ile Gly His Thr
820 825 830

Met Ala Ala Ala Gly Val Gly Gly Val Ile Lys Met Val Met Ala Leu
835 840 845

Arg Glu Gly Val Leu Pro Arg Thr Leu His Val Asp Lys Pro Ser Pro
850 855 860

Gln Val Asp Trp Ser Ala Gly Ala Val Arg Leu Leu Thr Glu Ala Val
865 870 875 880

Pro Trp Pro Gly Asp Ala Ala Gly Arg Leu Arg Arg Ala Gly Val Ser
885 890 895

Ser Phe Gly Ile Gly Gly Thr Asn Ala His Val Ile Leu Glu Glu Ala
900 905 910

Pro Ala Ala Gly Gly Cys Val Ala Gly Gly Gly Val Leu Glu Gly Ala
915 920 925

Pro Gly Leu Ala Ile Ser Val Ala Glu Ser Val Ala Ala Pro Val Ala
930 935 940

Val Ser Ala Pro Val Ala Glu Ser Val Pro Val Pro Val Pro Val Pro
945 950 955 960

Val Pro Val Pro Val Ser Ala Arg Ser Glu Ala Gly Leu Arg Ala Gln
965 970 975

Ala Glu Ala Leu Arg Gln Tyr Val Ala Val Arg Pro Asp Val Ser Leu
980 985 990

Ala Asp Val Gly Ala Gly Leu Ala Cys Gly Arg Ala Val Leu Glu His
995 1000 1005

Arg Ala Val Val Leu Ala Ala Asp Arg Glu Glu Leu Val Gln Gly Leu
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Gly Ala Leu Ala Ala Gly Glu Pro Asp Arg Arg Val Thr Thr Gly His
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Ala Pro Gly Gly Asp Arg Gly Gly Val Val Phe Val Phe Pro Gly Gln
1045 1050 1055

Gly Gly Gln Trp Ala Gly Met Gly Val Arg Leu Leu Ala Ser Ser Pro
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Val Phe Ala Arg Arg Met Gln Ala Cys Glu Glu Ala Leu Ala Pro Trp
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Val Ser Leu Ala Ala Leu Trp Arg Ser Tyr Gly Ile Glu Pro Asp Ala
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Val Leu Gly His Ser Gln Gly Glu Ile Ala Ala Ala His Val Cys Gly
1140 1145 1150

Ala Leu Ser Leu Lys Asp Ala Ala Lys Thr Val Ala Leu Arg Ser Arg
1155 1160 1165

Ala Leu Ala Ala Val Arg Gly Arg Gly Gly Met Ala Ser Val Pro Leu
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Pro Ala Gln Glu Val Glu Gln Leu Ile Gly Glu Arg Trp Ala Gly Arg
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Asp Ala Glu Ala Val Asp Glu Val Leu Ala Tyr Cys Ala Gly Thr Gly
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Val Arg Ala Arg Arg Ile Pro Val Asp Tyr Ala Ser His Cys Pro His
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Val Gln Pro Leu Arg Glu Glu Leu Leu Glu Leu Leu Gly Asp Ile Ser
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1265 1270 1275 1280

Leu Asp Thr Thr Thr Leu Asp Ala Ala Tyr Trp Tyr Arg Asn Leu His
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His Arg Val Phe Val Glu Val Ser Pro His Pro Thr Leu Val Pro Ala

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1345 1350 1355 1360

Ala His Thr His Thr Thr Gly Ile Gly Thr Pro Thr Thr Trp His His
1365 1370 1375

His Tyr Thr His His His Thr His Pro His Pro His Thr His Leu Asp
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Leu Pro Thr Tyr Pro Phe Gln His Gln His Tyr Trp Leu Glu Ser Ser
1395 1400 1405

Gln Pro Gly Ala Gly Ser Gly Ser Gly Ala Gly Ala Gly Ser Gly Ala
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Gly Ser Gly Arg Ala Gly Thr Ala Gly Gly Thr Ala Glu Val Glu Ser
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Arg Phe Trp Asp Ala Val Ala Arg Gln Asp Leu Glu Thr Val Ala Thr
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Thr Leu Ala Val Pro Pro Ser Ala Gly Leu Asp Thr Val Val Pro Ala
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Leu Ser Ala Trp His Arg His Gln His Asp Gln Ala Arg Ile Asn Thr
1475 1480 1485

Trp Thr Tyr Gln Glu Thr Trp Lys Pro Leu Thr Leu Pro Thr Thr His
1490 1495 1500

Gln Pro His Gln Thr Trp Leu Ile Ala Ile Pro Glu Thr Gln Thr His
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DEMANDE - 0961252

His Pro His Ile Thr Asn Ile Leu Thr Asn Leu His His His Gly Ile
1525 1530 1535

Thr Pro Ile Pro Leu Thr Leu Asn His Thr His Thr Asn Pro Gln His
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Leu His His Thr Leu His His Thr Arg Gln Gln Ala Gln Asn His Thr
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Thr Gly Ala Ile Thr Gly Leu Leu Ser Leu Leu Ala Leu Asp Glu Thr
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Pro His Pro His His Pro His Thr Pro Thr Gly Thr Leu Leu Asn Leu
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Thr Leu Thr Gln Thr His Thr Gln Thr His Pro Pro Thr Pro Leu Trp
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Tyr Ala Thr Thr Asn Ala Thr Thr Thr His Pro Asn Asp Pro Leu Thr
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His Pro Thr Gln Ala Gln Thr Trp Gly Leu Ala Arg Thr Thr Leu Leu
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Glu His Pro Thr His Thr Ala Gly Ile Ile Asp Leu Pro Thr Thr Pro
1650 1655 1660

Thr Pro His Thr Leu Gln His Leu Thr Gln Thr Leu Thr Gln Pro His
1665 1670 1675 1680

His Gln Thr Gln Leu Ala Ile Arg Thr Thr Gly Thr His Thr Arg Arg
1685 1690 1695

Leu Thr Pro Thr Thr Leu Thr Pro Thr His Gln Pro Pro Thr Pro Thr
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Pro His Gly Thr Thr Leu Ile Thr Gly Gly Thr Gly Ala Leu Ala Thr
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JP0514295.000210

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Thr Gln Leu Gln Gln Lys Gly Ile His Leu Thr Ile Thr Thr Cys Asp
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Thr Ser Asn Pro Asp Gln Leu Gln Gln Leu Leu Asn Thr Ile Pro Pro
1780 1785 1790

Gln His Pro Leu Thr Thr Val Ile His Thr Ala Gly Ile Leu Asp Asp
1795 1800 1805

Ala Thr Leu Thr Asn Leu Thr Pro Thr Gln Leu Asn Asn Val Leu Arg
1810 1815 1820

Ala Lys Ala His Ser Ala His Leu Leu His Gln Leu Thr Gln His Thr
1825 1830 1835 1840

Pro Leu Thr Ala Phe Val Leu Tyr Ser Ser Ala Ala Ala Thr Phe Gly
1845 1850 1855

Ala Pro Gly Gln Ala Asn Tyr Ala Ala Ala Asn Ala Tyr Leu Asp Ala
1860 1865 1870

Leu Ala His His Arg His Thr His His Leu Pro Ala Thr Ser Ile Ala
1875 1880 1885

Trp Gly Thr Trp Gln Gly Asn Gly Leu Ala Asp Ser Asp Lys Ala Arg
1890 1895 1900

Ala Tyr Leu Asp Arg Arg Gly Phe Arg Pro Met Ser Pro Glu Leu Ala
1905 1910 1915 1920

Thr Ala Ala Val Thr Gln Ala Ile Ala Asp Thr Glu Arg Pro Tyr Val

JP2004-536568-000147

1925 1930 1935

Val Ile Ala Asp Ile Asp Trp Ser Lys Ile Glu His Thr Ser Gln Thr
1940 1945 1950

Ser Asp Leu Val Ser Ala Ala Arg Glu Arg Glu Pro Ala Val Gln Arg
1955 1960 1965

Pro Thr Pro Pro Ala Glu Leu His Lys Thr Leu Ala His Gln Thr Ser
1970 1975 1980

Ala Asp Gln Arg Ala Ala Leu Leu Glu Leu Val Arg Asp His Val Ala
1985 1990 1995 2000

Ala Val Leu Arg His Ala Asp Pro Lys Ala Ile Ala Pro Asp Gln Ser
2005 2010 2015

Phe Arg Ala Leu Gly Phe Asp Ser Leu Thr Ala Val Glu Phe Arg Asn
2020 2025 2030

Leu Leu Ile Lys Ala Thr Gly Leu Arg Leu Pro Val Ser Leu Val Phe
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Asp His Pro Thr Pro Ala Lys Leu Ala Val His Leu Gln Asn Gln Leu
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Phe Pro Gly Gly Val Thr Ser Ala Asp Asp Phe Trp Asp Leu Ile Ser
2100 2105 2110

Ser Glu Gln Asp Ala Ile Gly Gly Phe Pro Thr Asp Arg Gly Trp Asp
2115 2120 2125

Leu Asp Thr Leu Tyr Asp Pro Asp Pro Asp His Pro Gly Thr Cys Tyr
2130 2135 2140

Thr Arg Asn Gly Gly Phe Leu Tyr Asp Ala Gly His Phe Asp Ala Glu
2145 2150 2155 2160

Phe Phe Gly Ile Ser Pro Arg Glu Ala Leu Ala Met Asp Pro Gln Gln
2165 2170 2175

Arg Leu Leu Leu Glu Thr Ala Trp Glu Thr Ile Glu His Ala Gly Ile
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Asn Pro His Thr Leu His Gly Thr Pro Thr Gly Val Phe Thr Gly Thr
2195 2200 2205

Asn Gly Gln Asp Tyr Ala Leu Arg Val His Asn Ala Gly Gln Ser Thr
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Asp Gly Phe Ala Leu Thr Gly Thr Ala Gly Ser Val Ile Ser Gly Arg
2225 2230 2235 2240

Ile Ser Tyr Thr Phe Gly Phe Glu Gly Pro Ala Val Ser Val Asp Thr
2245 2250 2255

Ala Cys Ser Ser Ser Leu Val Ala Leu His Leu Ala Cys Gln Ala Leu
2260 2265 2270

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2275 2280 2285

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2290 2295 2300

Ala Asp Gly His Cys Lys Ala Phe Ser Ala Ala Ala Asp Gly Thr Gly
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JP2004-535806-000151

His Arg Asn Gly His Arg Val Leu Ala Val Val Arg Gly Ser Ala Val
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Gln Gln Arg Val Ile Arg Gln Ala Leu Ala Asn Ala Gly Leu Ser Ala
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2420 2425 2430

His Thr Gln Ala Ala Ala Gly Val Ala Gly Val Ile Lys Met Val Met
2435 2440 2445

Ala Leu Arg His Gly Leu Leu Pro Arg Thr Leu His Val Asp Glu Pro
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Ser Pro His Val Asp Trp Ser Ala Gly Ala Val Gln Leu Leu Thr Glu
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Thr Val Pro Trp Pro Gly Gly Glu Gly Arg Leu Arg Arg Ala Gly Val
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Ser Ser Phe Gly Val Ser Gly Thr Asn Ala His Val Ile Leu Glu Glu
2500 2505 2510

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JP2004-525636-000150

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Gln Pro Ala Leu Phe Ala Phe Gln Val Ala Leu His Arg Leu Leu Thr
2705 2710 2715 2720

Asp Gly Tyr His Ile Thr Pro His Tyr Tyr Ala Gly His Ser Leu Gly
2725 2730 2735

Glu Ile Thr Ala Ala His Leu Ala Gly Ile Leu Thr Leu Thr Asp Ala
2740 2745 2750

Thr Thr Leu Ile Thr Gln Arg Ala Thr Leu Met Gln Thr Met Pro Pro
2755 2760 2765

Gly Thr Met Thr Thr Leu His Thr Thr Pro His His Ile Thr His His
2770 2775 2780

Leu Thr Ala His Glu Asn Asp Leu Ala Ile Ala Ala Ile Asn Thr Pro
2785 2790 2795 2800

Thr Ser Leu Val Ile Ser Gly Thr Pro His Thr Val Gln His Ile Thr
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Thr Leu Cys Gln Gln Gln Gly Ile Lys Thr Lys Thr Leu Pro Thr Asn
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His Ala Phe His Ser Pro His Thr Asn Pro Ile Leu Asn Gln Leu His
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Gln His Thr Gln Thr Leu Thr Tyr His Pro Pro His Thr Pro Leu Ile
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His Gln His Gly Val Thr Thr Tyr Ile Glu Leu Gly Pro Asp Asn Thr
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Leu Thr Leu Thr His Pro His His His Pro Gln Thr His Leu Leu Thr
2930 2935 2940

Applicant's Copy

Asn Leu Ala Lys Thr Thr Thr Thr Trp His Pro His His Tyr Thr His
2945 2950 2955 2960

His Asp Asn Gln Pro His Thr His Thr His Leu Asp Leu Pro Thr Tyr
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Pro Phe Gln His His His Tyr Trp Leu Glu Ser Thr Gln Pro Gly Ala
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2995 3000 3005

Gly Ala Thr Leu Glu Leu Ala Thr Asp Gly Gly Ala Leu Leu Ala Gly
3010 3015 3020

Arg Leu Ser Leu Arg Ser His Pro Trp Leu Ala Asp His Ala Val Gly
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Gly Thr Val Leu Leu Ser Gly Ala Thr Phe Leu Glu Leu Ala Leu His
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Ala Gly Thr Tyr Val Gly Cys Asp Arg Val Asp Glu Leu Thr Leu His
3060 3065 3070

Ala Pro Leu Val Val Pro Val Asp Gly Gly Val Ser Val Gln Val Gly
3075 3080 3085

Val Ala Ala Ala Asp Gly Glu Gly Arg Arg Leu Val Ser Val Tyr Ala
3090 3095 3100

Arg Gly Gly Ser Ala Cys Gly Gly Gly Gly Ala Ser Gly Gly Val Trp
3105 3110 3115 3120

Thr Cys His Ala Ser Gly Val Leu Val Glu Ala Ala Ala Gly Gly Val
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Val Val Asp Gly Leu Ala Gly Val Trp Pro Pro Arg Gly Ala Val Ala
3140 3145 3150

JP2005-095201A

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Leu Gly Pro Val Phe Ser Gly Leu Arg Ala Val Trp Arg Asp Gly Gly
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Asp Leu Leu Ala Glu Val Cys Leu Pro Glu Glu Ala Trp Gly Asp Ala
3185 3190 3195 3200

Ala Gly Phe Gly Leu His Pro Ala Leu Leu Asp Gly Val Val Gln Pro
3205 3210 3215

Leu Ser Val Leu Leu Pro Gly Gly Thr Gly Phe Gly Glu Gly Ala Gly
3220 3225 3230

Phe Gly Glu Gly Val Arg Val Pro Ala Val Trp Gly Gly Val Ser Leu
3235 3240 3245

His Arg Ala Gly Val Thr Gly Val Arg Val Arg Val Ser Ala Val Gly
3250 3255 3260

Arg Gly Gly Gly Arg Glu Ala Val Ser Val Val Val Gly Asp Glu Ala
3265 3270 3275 3280

Gly Val Pro Val Ala Ser Val Asp Arg Leu Glu Leu Arg Pro Val Asp
3285 3290 3295

Met Gly Gln Leu Arg Ala Val Ser Val Ser Ala Gly Arg Arg Gly Ser
3300 3305 3310

Leu Tyr Ala Val Gln Trp Ala Glu Val Gly Pro Val Pro Val Cys Gly
3315 3320 3325

Gln Ala Trp Ala Trp His Glu Asp Val Gly Glu Ser Gly Gly Gly Pro
3330 3335 3340

Val Pro Gly Val Val Val Leu Arg Cys Pro Asp Ala Gly Ala Gly Gly

JP2005-095150-000154

3345 3350 3355 3360

Gly Gly Gly Gly Gly Gly Gly Gly Gly Val Gly Glu Val Val Gly Gly
3365 3370 3375

Val Leu Gly Val Val Gln Gly Trp Leu Gly Leu Glu Arg Phe Ala Gly
3380 3385 3390

Ser Arg Leu Val Val Val Thr Arg Gly Ala Val Val Ala Gly Pro Glu
3395 3400 3405

Asp Gly Pro Val Asp Val Val Gly Ala Ser Val Trp Gly Leu Val Arg
3410 3415 3420

Ser Ala Gln Ala Glu His Pro Asp Arg Phe Val Leu Leu Asp Leu Asp
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Thr Asp Thr Gly Thr Asp Leu Asp Thr Gly Ala Gly Ala Gly Trp Gly
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Val Asp Gly Gly Arg Val Ala Ala Val Val Ala Cys Gly Glu Pro Gln
3460 3465 3470

Leu Ala Val Arg Gly Glu Arg Leu Leu Ala Ala Arg Leu Lys Arg Leu
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Glu Ser Ser Gly Asp Val Pro Ala Gln Arg Ser Gly Asp Thr Arg Ala
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Arg Arg Ser Asp Val Pro Ala Gln Arg Ser Gly Gly Val Pro Ala Arg
3505 3510 3515 3520

Arg Ser Val Asp Val Ser Gly Arg Glu Val Leu Pro Trp Leu Ser Gly
3525 3530 3535

Gly Ser Val Leu Val Thr Gly Gly Thr Gly Val Leu Gly Ala Ala Val
3540 3545 3550

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Ala Arg His Leu Ala Gly Val Cys Gly Val Arg Asp Leu Leu Leu Val
3555 3560 3565

Ser Arg Arg Gly Pro Asp Ala Pro Gly Ala Glu Gly Leu Arg Ala Glu
3570 3575 3580

Leu Ala Ala Leu Gly Ala Glu Val Arg Ile Val Ala Cys Asp Val Gly
3585 3590 3595 3600

Glu Arg Arg Glu Val Val Arg Leu Leu Glu Gly Val Pro Ala Gly Cys
3605 3610 3615

Pro Leu Thr Gly Val Val His Ala Ala Gly Val Leu Asp Asp Ala Thr
3620 3625 3630

Ile Ala Ser Leu Thr Pro Glu Arg Leu Gly Thr Val Phe Ala Ala Lys
3635 3640 3645

Val Asp Ala Ala Leu Leu Leu Asp Glu Leu Thr Arg Gly Met Glu Leu
3650 3655 3660

Ser Ala Phe Val Leu Phe Ser Ser Ala Ala Gly Ile Leu Gly Ser Ala
3665 3670 3675 3680

Gly Gln Gly Asn Tyr Ala Ala Ala Asn Ala Ala Leu Asp Ala Leu Ala
3685 3690 3695

Tyr Arg Arg Arg Ala Ala Gly Leu Pro Gly Val Ser Leu Ala Trp Gly
3700 3705 3710

Leu Trp Glu Glu Ala Ser Gly Met Thr Gly His Leu Ala Gly Thr Asp
3715 3720 3725

His Arg Arg Ile Ile Arg Ser Gly Leu His Pro Met Ser Thr Pro Asp
3730 3735 3740

Ala Leu Ala Leu Phe Asp Ala Ala Leu Ala Leu Asp Arg Pro Val Leu
3745 3750 3755 3760

Leu Pro Ala Asp Leu Arg Pro Ala Pro Pro Leu Pro Pro Leu Leu Gln
3765 3770 3775

Asp Leu Leu Pro Ala Thr Arg Arg Arg Thr Thr Arg Thr Thr Thr Thr
3780 3785 3790

Gly Gly Ala Asp Asn Gly Ala Gln Leu His Ala Arg Leu Ala Gly Gln
3795 3800 3805

Thr His Glu Gln Gln His Thr Thr Leu Leu Ala Leu Val Arg Ser His
3810 3815 3820

Ile Ala Thr Val Leu Gly His Thr Thr Pro Asp Thr Ile Pro Pro Asp
3825 3830 3835 3840

Arg Ala Phe Arg Asp Leu Gly Phe Asp Ser Leu Thr Ala Val Glu Leu
3845 3850 3855

Arg Asn Arg Leu Ser Arg Thr Thr Gly Leu Arg Leu Pro Thr Thr Leu
3860 3865 3870

Ala Phe Asp His Pro Asn Pro Thr Thr Leu Thr His His Leu His Thr
3875 3880 3885

Gln Leu Gln Pro Gln Pro Asp Asn Ala Val Ala Pro Val Leu Ala Glu
3890 3895 3900

Leu Asp Lys Leu Glu Ser Ala Leu Ser Ala Leu Asp Lys Thr Asp Ser
3905 3910 3915 3920

Ala Ser Glu Arg Val Thr Leu Arg Leu Lys Ser Leu Met Leu Arg Trp
3925 3930 3935

Asn Ala Pro Gln His Pro Thr Ala Glu Ser Ala Asp Asp Asp Glu Lys
3940 3945 3950

Phe Thr Ser Ala Thr Glu Ala Glu Ile Phe Lys Phe Ile Asp Asn Asp

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3955 3960 3965

Leu Gly Leu Ser
3970

<210> 4
<211> 6239
<212> PRT
<213> Streptomyces avermitilis

<400> 4
Met Gln Leu Ala Asn Glu Ala Lys Leu Leu Glu Tyr Leu Lys Arg Val
1 5 10 15

Thr Ala Asp Leu Asp Arg Thr Arg Arg Arg Leu Tyr Glu Val Val Glu
20 25 30

Arg Glu Gln Glu Pro Ile Ala Ile Val Gly Met Ala Cys Arg Tyr Pro
35 40 45

Gly Gly Ala Thr Ser Pro Thr Arg Leu Trp His Leu Val Lys Ser Gln
50 55 60

Thr Asp Ala Ile Gly Glu Phe Pro Thr Asp Arg Gly Trp Asn Leu Glu
65 70 75 80

Gln Leu Tyr Asp Pro Asp Pro Asp Arg Ser Gly Thr Ser Tyr Thr Arg
85 90 95

Ser Gly Gly Phe Leu Tyr Asp Ala Gly Asp Phe Asp Ala Ala Phe Phe
100 105 110

Glu Leu Ser Pro Arg Glu Ala Leu Ala Met Asp Pro Gln Gln Arg Leu
115 120 125

Leu Leu Glu Thr Thr Trp Glu Thr Phe Glu Gln Gly Gly Ile Asp Pro
130 135 140

Arg Ser Met Arg Gly Ser Arg Thr Gly Val Phe Val Gly Ile Asn Pro
145 150 155 160

Glu Asp Tyr Thr Thr Gly Tyr Thr His Gln Pro Ser Asn Ala Val Glu
165 170 175

Gly Tyr Leu Leu Thr Gly Ser Ala Ala Ser Ile Ala Ser Gly Arg Ile
180 185 190

Ser Tyr Asn Phe Gly Leu Glu Gly Pro Ala Ile Thr Ile Asp Thr Ala
195 200 205

Cys Ser Ser Ser Leu Val Ala Leu His Leu Ala Cys Gln Ala Leu Arg
210 215 220

Ser Gly Glu Cys Thr Met Ala Leu Ala Gly Gly Ala Ser Val Met Ala
225 230 235 240

Thr Pro Phe Val Phe Thr Glu Phe Ser Arg Gln Arg Gly Leu Ala Ala
245 250 255

Asp Gly Arg Cys Lys Ala Phe Ser Ala Ala Ala Asp Gly Thr Gly Trp
260 265 270

Ser Glu Gly Val Gly Met Leu Leu Val Glu Arg Leu Ser Asp Ala Arg
275 280 285

Arg Asn Gly His Arg Val Leu Ala Val Val Arg Gly Ser Ala Val Asn
290 295 300

Gln Asp Gly Ala Ser Asn Gly Leu Thr Ala Pro Asn Gly Arg Ser Gln
305 310 315 320

Val Lys Val Ile Arg Gln Ala Leu Ala Asn Ala His Leu Ser Pro Ala
325 330 335

Asp Val Asp Ala Val Glu Ala His Gly Thr Gly Thr Thr Leu Gly Asp

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340 345 350

Pro Ile Glu Ala Gln Ala Leu Val Glu Ala Tyr Gly Gln Asp Arg Pro
355 360 365

Asn Gly Arg Pro Leu Trp Leu Gly Thr Leu Lys Ser Asn Ile Gly His
370 375 380

Ser Met Ala Ala Ala Gly Val Gly Gly Val Ile Lys Met Val Met Ala
385 390 395 400

Leu Arg Asn Gly Leu Leu Pro Arg Thr Leu His Val Asp Glu Pro Ser
405 410 415

Pro His Val Asp Trp Ser Ala Gly Ala Val Gln Leu Leu Thr Glu Thr
420 425 430

Val Pro Trp Pro Gly Gly Glu Gly Arg Leu Arg Arg Ala Gly Val Ser
435 440 445

Ser Phe Gly Val Ser Gly Thr Asn Ala His Val Ile Leu Glu Glu Ala
450 455 460

Pro Ala His Asn Ile Pro Ser Asp Thr Pro Ala Asp Asp Val Pro Gly
465 470 475 480

Glu Ser Ala Ala Asp Glu Asp Ala Gly Ser Gly Asp Glu Ala Ala Ala
485 490 495

Gly Ser Pro Gly Val Trp Pro Trp Leu Val Ser Ala Lys Ser Gln Pro
500 505 510

Ala Leu Arg Ala Gln Ala Gln Ala Leu His Ala His Leu Thr Asp His
515 520 525

Pro Gly Leu Asp Leu Ala Asp Val Gly Tyr Thr Leu Ala His Ala Arg
530 535 540

Ala Val Phe Asp His Arg Ala Thr Leu Ile Ala Ala Asp Arg Asp Thr
545 550 555 560

Phe Leu Gln Ala Leu Gln Ala Leu Ala Ala Gly Glu Pro His Pro Ala
565 570 575

Val Ile His Ser Ser Ala Pro Gly Gly Thr Gly Thr Gly Glu Ala Ala
580 585 590

Gly Lys Thr Ala Phe Ile Cys Ser Gly Gln Gly Thr Gln Arg Pro Gly
595 600 605

Met Ala His Gly Leu Tyr His Thr His Pro Val Phe Ala Ala Ala Leu
610 615 620

Asn Asp Ile Cys Thr His Leu Asp Pro His Leu Asp His Pro Leu Leu
625 630 635 640

Pro Leu Leu Thr Gln Asp Pro Asn Thr Gln Asp Thr Thr Thr Leu Glu
645 650 655

Glu Ala Ala Ala Leu Leu Gln Gln Thr Arg Tyr Ala Gln Pro Ala Leu
660 665 670

Phe Ala Phe Gln Val Ala Leu His Arg Leu Leu Thr Asp Gly Tyr His
675 680 685

Ile Thr Pro His Tyr Tyr Ala Gly His Ser Leu Gly Glu Ile Thr Ala
690 695 700

Ala His Leu Ala Gly Ile Leu Thr Leu Thr Asp Ala Thr Thr Leu Ile
705 710 715 720

Thr Gln Arg Ala Thr Leu Met Gln Thr Met Pro Pro Gly Thr Met Thr
725 730 735

Thr Leu His Thr Thr Pro His His Ile Thr His His Leu Thr Ala His
740 745 750

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Glu Asn Asp Leu Ala Ile Ala Ala Ile Asn Thr Pro Thr Ser Leu Val
755 760 765

Ile Ser Gly Thr Pro His Thr Val Gln His Ile Thr Thr Leu Cys Gln
770 775 780

Gln Gln Gly Ile Lys Thr Lys Thr Leu Pro Thr Asn His Ala Phe His
785 790 795 800

Ser Pro His Thr Asn Pro Ile Leu Asn Gln Leu His Gln His Thr Gln
805 810 815

Thr Leu Thr Tyr His Pro Pro His Thr Pro Leu Ile Thr Ala Asn Thr
820 825 830

Pro Pro Asp Gln Leu Leu Thr Pro His Tyr Trp Thr Gln Gln Ala Arg
835 840 845

Asn Thr Val Asp Tyr Ala Thr Thr Thr Gln Thr Leu His Gln His Gly
850 855 860

Val Thr Thr Tyr Ile Glu Leu Gly Pro Asp Asn Thr Leu Thr Thr Leu
865 870 875 880

Thr His Asp Asn Leu Pro Asn Thr Pro Thr Thr Thr Leu Thr Leu Thr
885 890 895

His Pro His His His Pro Gln Thr His Leu Leu Thr Asn Leu Ala Lys
900 905 910

Thr Thr Thr Thr Trp His Pro His His Tyr Thr His His His Asn Gln
915 920 925

Pro His Thr His Thr His Leu Asp Leu Pro Thr Tyr Pro Phe Gln His
930 935 940

His His Tyr Trp Leu Gln Pro Pro Gly Lys Pro Ser Asp Pro Ser Pro

945 950 955 960

Ser Glu Gly Arg Glu Gln Ala Thr Thr Pro Ser Thr Pro Leu Arg Asp
965 970 975

Val Leu Val Gly Lys Ser Pro Gln Glu Arg Asp Glu Glu Leu Leu Arg
980 985 990

Leu Val Arg Thr His Ala Ala Ala Val Leu Gly His Ala Thr Pro Glu
995 1000 1005

Val Ile Val Pro Asn Lys Ala Phe Lys Glu Leu Gly Phe Asp Ser Leu
1010 1015 1020

Ala Ala Ile Gln Leu Arg Asn Arg Leu Leu Ala Asp Val Asp Leu Pro
1025 1030 1035 1040

Leu Pro Ala Thr Leu Ile Phe Asp Tyr Pro Thr Pro Met Ala Leu Cys
1045 1050 1055

Gln Phe Leu Arg Ala Ala Ile Val Gly Ala Asp Thr Gly Thr Thr Thr
1060 1065 1070

Arg Leu Pro Leu Thr Ala Val Pro Ala Asp Glu Pro Ile Ala Ile Val
1075 1080 1085

Gly Met Ala Cys Arg Tyr Pro Gly Asp Val Arg Thr Val Asp Asp Leu
1090 1095 1100

Trp Gln Val Val Ser Gly Gly His Asp Ala Ile Gly Gly Phe Pro Thr
1105 1110 1115 1120

Asn Arg Gly Trp Asp Leu Asp Thr Leu Tyr Asn Pro Asp Pro Asp His
1125 1130 1135

His Gly Thr Ser Tyr Thr Arg Ser Gly Gly Phe Leu Tyr Asp Ala Gly
1140 1145 1150

Asn Phe Asp Pro Asp Phe Phe Gly Ile Ser Pro Arg Glu Ala Leu Ala
1155 1160 1165

Met Asp Pro Gln Gln Arg Leu Leu Leu Glu Thr Ala Trp Glu Ser Ile
1170 1175 1180

Glu His Ala Cys Ile Asn Pro Asp Ser Leu Arg Gly Thr Pro Thr Gly
1185 1190 1195 1200

Val Phe Ala Gly Leu Thr Tyr His Asp Tyr Ala Ala Arg Phe Pro Thr
1205 1210 1215

Ala Pro Ala Gly Phe Glu Gly Tyr Leu Gly His Gly Ser Ala Gly Ser
1220 1225 1230

Ile Ala Ser Gly Arg Val Ala Tyr Ala Leu Gly Leu Glu Gly Pro Ala
1235 1240 1245

Leu Thr Val Asp Thr Ala Cys Ser Ser Ser Leu Val Ala Leu His Leu
1250 1255 1260

Ala Cys Gln Ala Leu Arg Ser Gly Glu Cys Ser Met Ala Leu Ala Gly
1265 1270 1275 1280

Gly Val Thr Val Met Ser Thr Pro Ala Gly Phe Val Glu Phe Ser Arg
1285 1290 1295

Gln Arg Gly Leu Ala Val Asp Gly Arg Cys Lys Ala Phe Ser Ala Ala
1300 1305 1310

Ala Asp Gly Thr Gly Trp Gly Glu Gly Val Gly Met Leu Leu Val Glu
1315 1320 1325

Arg Leu Ser Asp Ala Arg Arg Leu Gly His Arg Ile Leu Ala Val Val
1330 1335 1340

Arg Gly Ser Ala Val Asn Gln Asp Gly Ala Ser Asn Gly Leu Thr Ala
1345 1350 1355 1360

Pro Asn Gly Pro Ser Gln Glu Arg Val Ile Arg Leu Ala Leu Ala Asn
1365 1370 1375

Ala Asp Leu Thr Pro Ala Asp Val Asp Ala Val Glu Ala His Gly Thr
1380 1385 1390

Gly Thr Thr Leu Gly Asp Pro Ile Glu Ala Gln Ala Leu Leu Ala Thr
1395 1400 1405

Tyr Gly Gln Asp Arg Pro Gly Asn Glu Pro Leu Trp Leu Gly Ser Met
1410 1415 1420

Lys Ser Asn Ile Gly His Ala Gln Ala Ala Ala Gly Val Gly Gly Val
1425 1430 1435 1440

Ile Lys Met Val Met Ala Leu Arg Asn Gly Leu Leu Pro Arg Thr Leu
1445 1450 1455

His Val Asp Glu Pro Ser Pro His Val Asp Trp Ser Ala Gly Ala Val
1460 1465 1470

Gln Leu Leu Thr Glu Thr Val Pro Trp Pro Gly Gly Glu Gly Arg Leu
1475 1480 1485

Arg Arg Ala Gly Val Ser Ser Phe Gly Val Ser Gly Thr Asn Ala His
1490 1495 1500

Val Ile Leu Glu Glu Ala Pro Ala His Asn Ile Pro Ser Asp Thr Pro
1505 1510 1515 1520

Ala Asp Asp Ala Pro Gly Glu Ala Ala Ala Asp Asp Val Pro Gly Glu
1525 1530 1535

Ala Ala Gly Asp Asp Ala Gly Thr Gly Gly Glu Ala Thr Gly Pro Ala
1540 1545 1550

Ala Gly Ser Pro Gly Val Trp Pro Trp Leu Val Ser Ala Lys Ser Gln

1555 1560 1565

Pro Ala Leu Arg Ala Gln Ala Gln Ala Leu His Ala His Leu Thr Asp
1570 1575 1580

His Pro Gly Leu Asp Leu Ala Asp Val Gly Tyr Thr Leu Ala His Ala
1585 1590 1595 1600

Arg Ala Val Phe Asp His Arg Ala Thr Leu Ile Ala Ala Asp Arg Asp
1605 1610 1615

Thr Phe Leu Gln Ala Leu Gln Ala Leu Ala Ala Gly Glu Pro His Pro
1620 1625 1630

Ala Val Ile His Ser Ser Ala Pro Gly Gly Thr Gly Thr Gly Glu Ala
1635 1640 1645

Ala Gly Lys Thr Ala Phe Ile Cys Ser Gly Gln Gly Thr Gln Arg Pro
1650 1655 1660

Gly Met Ala His Gly Leu Tyr His Thr His Pro Val Phe Ala Ala Ala
1665 1670 1675 1680

Leu Asn Asp Ile Cys Thr His Leu Asp Pro His Leu Asp His Pro Leu
1685 1690 1695

Leu Pro Leu Leu Thr Gln Asp Pro Asn Thr Gln Asp Thr Thr Thr Leu
1700 1705 1710

Glu Glu Ala Ala Ala Leu Leu Gln Gln Thr Pro Tyr Ala Gln Pro Ala
1715 1720 1725

Leu Phe Ala Phe Gln Val Ala Leu His Arg Leu Leu Thr Asp Gly Tyr
1730 1735 1740

His Ile Thr Pro His Tyr Tyr Ala Gly His Ser Leu Gly Glu Ile Thr
1745 1750 1755 1760

Ala Ala His Leu Ala Gly Ile Leu Thr Leu Thr Asp Ala Thr Thr Leu
1765 1770 1775

Ile Thr Gln Arg Ala Thr Leu Met Gln Thr Met Pro Pro Gly Thr Met
1780 1785 1790

Thr Thr Leu His Thr Thr Pro His His Ile Thr His His Leu Thr Ala
1795 1800 1805

His Glu Asn Asp Leu Ala Ile Ala Ala Ile Asn Thr Pro Thr Ser Leu
1810 1815 1820

Val Ile Ser Gly Thr Pro His Thr Val Gln His Ile Thr Thr Leu Cys
1825 1830 1835 1840

Gln Gln Gln Gly Ile Lys Thr Lys Thr Leu Pro Thr Lys Asn Ala Phe
1845 1850 1855

His Ser Pro His Thr Asn Pro Ile Leu Asn Gln Leu His Gln His Thr
1860 1865 1870

Gln Thr Leu Thr Tyr His Pro Pro His Thr Pro Leu Ile Thr Ala Asn
1875 1880 1885

Thr Pro Pro Asp Gln Leu Leu Thr Pro His Tyr Trp Thr Gln Gln Ala
1890 1895 1900

Arg Asn Thr Val Asp Tyr Ala Thr Thr Thr Gln Thr Leu His Gln His
1905 1910 1915 1920

Gly Val Thr Thr Tyr Ile Glu Leu Gly Pro Asp Asn Thr Leu Thr Thr
1925 1930 1935

Leu Thr His His Asn Leu Pro Asn Thr Pro Thr Thr Thr Leu Thr Leu
1940 1945 1950

Thr His Pro His His His Pro Gln Thr His Leu Leu Thr Asn Leu Ala
1955 1960 1965

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Lys Thr Thr Thr Thr Trp His Pro His His Tyr Thr His His His Asn
1970 1975 1980

Gln Pro His Thr His Thr His Leu Asp Leu Pro Thr Tyr Pro Phe Gln
1985 1990 1995 2000

His Gln His Tyr Trp Leu Glu Ser Thr Gln Pro Gly Ala Gly Ser Gly
2005 2010 2015

Ser Gly Ser Gly Ser Gly Arg Ala Gly Thr Ala Gly Gly Thr Ala Glu
2020 2025 2030

Val Glu Ser Arg Phe Trp Asp Ala Val Ala Arg Gln Asp Leu Glu Thr
2035 2040 2045

Val Ala Thr Thr Leu Ala Val Pro Pro Ser Ala Gly Leu Asp Thr Val
2050 2055 2060

Val Pro Ala Leu Ser Ala Trp His Arg His Gln His Asp Gln Ala Arg
2065 2070 2075 2080

Ile Asn Thr Trp Thr Tyr Gln Glu Thr Trp Lys Pro Leu Thr Leu Pro
2085 2090 2095

Thr Thr His Gln Pro His Gln Thr Trp Leu Ile Ala Ile Pro Glu Thr
2100 2105 2110

Gln Thr His His Pro His Ile Thr Asn Ile Leu Thr Asn Leu His His
2115 2120 2125

His Gly Ile Thr Pro Ile Pro Leu Thr Leu Asn His Thr His Thr Asn
2130 2135 2140

Pro Gln His Leu His His Thr Arg Gln Gln Ala Gln Asn His Thr Thr
2145 2150 2155 2160

Gly Pro Ile Thr Gly Leu Leu Ser Leu Leu Ala Leu Asp Glu Thr Pro

2165 2170 2175

His Pro His His Pro His Thr Pro Thr Gly Thr Leu Leu Asn Leu Thr
2180 2185 2190

Leu Thr Gln Thr His Thr Gln Thr His Pro Pro Thr Pro Leu Trp Tyr
2195 2200 2205

Ala Thr Thr Asn Ala Thr Thr Thr His Pro Asn Asp Pro Leu Thr His
2210 2215 2220

Pro Thr Gln Ala Gln Thr Trp Gly Leu Ala Arg Thr Thr Leu Leu Glu
2225 2230 2235 2240

His Pro Thr His Thr Ala Gly Ile Ile Asp Leu Pro Thr Thr Pro Thr
2245 2250 2255

Pro His Thr Leu His His Leu Thr Gln Thr Leu Thr Gln Pro His His
2260 2265 2270

Gln Thr Gln Leu Ala Ile Arg Thr Thr Gly Thr His Thr Arg Arg Leu
2275 2280 2285

Thr Pro Thr Thr Leu Thr Pro Thr His Gln Pro Pro Thr Pro Thr Pro
2290 2295 2300

His Gly Thr Thr Leu Ile Thr Gly Gly Thr Gly Ala Leu Ala Thr His
2305 2310 2315 2320

Leu Thr His His Leu Thr Thr His Gln Pro Thr Gln His Leu Leu Leu
2325 2330 2335

Thr Ser Arg Thr Gly Pro His Thr Pro His Ala Gln His Leu Thr Thr
2340 2345 2350

Gln Leu Gln Gln Lys Gly Ile His Leu Thr Ile Thr Thr Cys Asp Thr
2355 2360 2365

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Ser Asn Pro Asp Gln Leu Gln Gln Leu Leu Asn Thr Ile Pro Pro Gln
2370 2375 2380

His Pro Leu Thr Thr Val Ile His Thr Ala Gly Ile Leu Asp Asp Ala
2385 2390 2395 2400

Thr Leu Thr Asn Leu Thr Pro Thr Gln Leu Asn Asn Val Leu Arg Ala
2405 2410 2415

Lys Ala His Ser Ala His Leu Leu His Gln Leu Thr Gln His Thr Pro
2420 2425 2430

Leu Asn Ala Phe Val Leu Tyr Ser Ser Ala Ala Ala Thr Phe Gly Ala
2435 2440 2445

Pro Gly Gln Ala Asn Tyr Ala Ala Ala Asn Ala Tyr Leu Asp Ala Leu
2450 2455 2460

Ala His His Arg His Thr His His Leu Pro Ala Thr Ser Ile Ala Trp
2465 2470 2475 2480

Gly Thr Trp Gln Gly Asn Gly Leu Ala Thr Gly Gln Val Ser Glu His
2485 2490 2495

Leu Arg Arg Arg Gly Met Phe Ala Met Pro Pro Glu Leu Ala Val Thr
2500 2505 2510

Ala Val Asp Gly Ala Ile Ala Ser Gly Arg Pro Ser Leu Leu Val Ala
2515 2520 2525

Asp Ile Asp Trp Lys Lys Leu Gly Pro Val Leu Ser Ser Lys Ser Ser
2530 2535 2540

Val Leu Leu Glu Asp Leu Pro Gln Ala Gln Gly Thr Glu Glu Ala Arg
2545 2550 2555 2560

Ser Thr Val Glu Gln Thr Glu Ser Thr Asn Leu Arg Gln Leu Leu Met
2565 2570 2575

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Gly Arg Ser Arg Ser Glu Gln Glu Glu Glu Leu Leu Ser Leu Val Arg
2580 2585 2590

Ile His Ser Ala Ala Val Leu Gly Arg Asp Asp Ser Glu Ala Ile Pro
2595 2600 2605

Pro Gly Arg Leu Phe Arg Asp Leu Gly Phe Asp Ser Leu Ala Ala Val
2610 2615 2620

Glu Leu Arg Asn His Leu Ala Ala Gln Thr Glu Leu Ala Leu Pro Thr
2625 2630 2635 2640

Thr Leu Val Phe Asp Tyr Pro Ser Pro Thr Lys Leu Ala Gln Phe Leu
2645 2650 2655

Leu Ser Glu Ile Ala Glu Phe Gln Pro Asp Asn Ser Thr Pro Leu Pro
2660 2665 2670

Arg Pro Arg Ala Glu Leu Asp Glu Pro Ile Ala Ile Val Gly Met Ala
2675 2680 2685

Cys Arg Phe Pro Gly Gly Val Thr Ser Ala Asp Asp Phe Trp Asp Leu
2690 2695 2700

Ile Ser Ser Glu Gln Asp Ala Ile Gly Gly Phe Pro Thr Asp Arg Gly
2705 2710 2715 2720

Trp Asp Leu Asp Thr Leu Tyr Asp Pro Asp Pro Asp His Pro Gly Thr
2725 2730 2735

Cys Tyr Thr Arg Asn Gly Gly Phe Leu Tyr Asp Ala Gly His Phe Asp
2740 2745 2750

Ala Glu Phe Phe Gly Ile Ser Pro Arg Glu Ala Leu Ala Met Asp Pro
2755 2760 2765

Gln Gln Arg Leu Leu Leu Glu Thr Ala Trp Glu Thr Ile Glu His Ala

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2770 2775 2780

Gly Ile Asn Pro His Thr Leu His Gly Thr Pro Thr Gly Val Phe Thr
2785 2790 2795 2800

Gly Thr Asn Gly Gln Asp His Ala Ala His Ile Arg Gln Ala Pro Ser
2805 2810 2815

Gly Thr Glu Gly Phe Val Leu Thr Gly Ala Ala Thr Ser Ile Ala Ser
2820 2825 2830

Gly Arg Ile Ser Tyr Ile Leu Gly Leu Glu Gly Pro Ala Val Thr Leu
2835 2840 2845

Asp Thr Ala Cys Ser Ser Ser Leu Val Ala Leu His Leu Ala Cys Gln
2850 2855 2860

Ser Leu Arg Ser Gly Glu Cys Thr Met Ala Leu Ala Gly Gly Ala Thr
2865 2870 2875 2880

Val Met Thr Thr Pro Ile Thr Phe Thr Glu Phe Ala Arg Gln Arg Gly
2885 2890 2895

Leu Ala Pro Asp Gly Arg Cys Lys Ala Phe Ser Ala Ala Ala Asp Gly
2900 2905 2910

Thr Gly Trp Gly Glu Gly Val Gly Met Leu Leu Val Glu Arg Leu Ser
2915 2920 2925

Asp Ala Arg Arg Asn Gly His Arg Val Leu Ala Val Val Arg Gly Ser
2930 2935 2940

Ala Val Asn Gln Asp Gly Ala Ser Asn Gly Leu Thr Ala Pro Asn Gly
2945 2950 2955 2960

Pro Ser Gln Gln Arg Val Ile Arg Gln Ala Leu Ala Asn Ala Asp Leu
2965 2970 2975

Thr Pro Ala Asp Val Asp Ala Val Glu Ala His Gly Thr Gly Thr Thr
2980 2985 2990

Leu Gly Asp Pro Ile Glu Ala Gln Ala Ile Leu Ala Thr Tyr Gly Gln
2995 3000 3005

Asp Arg Pro Gly Asn Gly Pro Leu Trp Leu Gly Ser Val Lys Ser Asn
3010 3015 3020

Val Gly His Thr Gln Ala Ala Ala Gly Val Ala Gly Val Ile Lys Met
3025 3030 3035 3040

Val Met Ala Leu Arg His Arg Thr Leu Pro Pro Thr Leu His Ala Asp
3045 3050 3055

Glu Pro Ser Pro His Val Asp Trp Ser Ala Gly Ala Val Gln Leu Leu
3060 3065 3070

Thr Glu Thr Val Pro Trp Pro Gly Gly Glu Gly Arg Pro Arg Arg Ala
3075 3080 3085

Gly Val Ser Ser Phe Gly Val Ser Gly Thr Asn Ala His Val Ile Leu
3090 3095 3100

Glu Glu Ala Pro Ala Asp Asp Val Pro Gly Gly Pro Pro Ala Asp Glu
3105 3110 3115 3120

Asp Ala Gly Ser Gly Glu Glu Ala Ala Ala Gly Ser Pro Gly Val Trp
3125 3130 3135

Pro Trp Leu Val Ser Ala Lys Ser Gln Pro Ala Leu Arg Ala Gln Ala
3140 3145 3150

Gln Ala Leu His Ala His Leu Thr Asp His Pro Gly Leu Asp Leu Ala
3155 3160 3165

Asp Val Gly Tyr Thr Leu Ala His Ala Arg Ala Val Phe Asp His Arg
3170 3175 3180

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Ala Thr Leu Ile Ala Ala Asp Arg Asp Thr Phe Leu Gln Ala Leu Gln
3185 3190 3195 3200

Ala Leu Ala Ala Gly Glu Pro His Pro Ala Val Ile His Ser Ser Ala
3205 3210 3215

Pro Gly Gly Thr Gly Thr Gly Glu Ala Ala Gly Lys Thr Ala Phe Ile
3220 3225 3230

Cys Ser Gly Gln Gly Thr Gln Arg Pro Gly Met Ala His Gly Leu Tyr
3235 3240 3245

His Thr His Pro Val Phe Ala Ala Ala Leu Asn Asp Ile Cys Thr His
3250 3255 3260

Leu Asp Pro His Leu Asp His Pro Leu Leu Pro Leu Leu Thr Gln Asn
3265 3270 3275 3280

Asp Asn Asp Asn Asp Asn Glu Asp Ala Ala Ala Leu Leu Gln Gln Thr
3285 3290 3295

Pro Tyr Ala Gln Pro Ala Leu Phe Ala Phe Gln Val Ala Leu His Arg
3300 3305 3310

Leu Leu Thr Asp Gly Tyr His Ile Thr Pro His Tyr Tyr Ala Gly His
3315 3320 3325

Ser Leu Gly Glu Ile Thr Ala Ala His Leu Ala Gly Ile Leu Thr Leu
3330 3335 3340

Thr Asp Ala Thr Thr Leu Ile Thr Gln Arg Ala Thr Leu Met Gln Thr
3345 3350 3355 3360

Met Pro Pro Gly Thr Met Thr Thr Leu His Thr Thr Pro His His Ile
3365 3370 3375

Thr His His Leu Thr Ala His Glu Asn Asp Leu Ala Ile Ala Ala Ile

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3380 3385 3390

Asn Thr Pro Thr Ser Leu Val Ile Ser Gly Thr Pro His Thr Val Gln
3395 3400 3405

His Ile Thr Thr Leu Cys Gln Gln Gln Gly Ile Lys Thr Lys Thr Leu
3410 3415 3420

Pro Thr Asn His Ala Phe His Ser Pro His Thr Asn Pro Ile Leu Asn
3425 3430 3435 3440

Gln Leu His Gln His Thr Gln Thr Leu Thr Tyr His Pro Pro His Thr
3445 3450 3455

Pro Leu Ile Thr Ala Asn Thr Pro Pro Asp Gln Leu Leu Thr Pro His
3460 3465 3470

Tyr Trp Thr Gln Gln Ala Arg Asn Thr Val Asp Tyr Ala Thr Thr Thr
3475 3480 3485

Gln Thr Leu His Gln His Gly Val Thr Thr Tyr Ile Glu Leu Gly Pro
3490 3495 3500

Asp Asn Thr Leu Thr Thr Leu Thr His His Asn Leu Pro Asn Thr Pro
3505 3510 3515 3520

Thr Thr Thr Leu Thr Leu Thr His Pro His His His Pro Gln Thr His
3525 3530 3535

Leu Leu Thr Asn Leu Ala Lys Thr Thr Thr Thr Trp His Pro His His
3540 3545 3550

Tyr Thr His His His Asn Gln Pro His Thr His Thr His Leu Asp Leu
3555 3560 3565

Pro Thr Tyr Pro Phe Gln His His His Tyr Trp Leu Glu Leu Pro Ser
3570 3575 3580

EP 0 954 525 B1

Ala Gln Thr Ser Pro Gly Gln Arg Arg Ser Arg Arg Ser Ala Pro Asp
3585 3590 3595 3600

Thr Ala Glu Ser Glu Phe Trp Asp Ala Val Asn Glu Glu Asp Leu Gln
3605 3610 3615

Ser Leu Ala Glu Thr Leu Asp Ile Asp Ala Ser Ala Leu Asp Thr Val
3620 3625 3630

Val Pro Ala Leu Ser Ala Trp His Arg His Gln His Asp Gln Ala Arg
3635 3640 3645

Ile Asn Thr Trp Thr Tyr Gln Glu Thr Trp Lys Pro Leu Thr Leu Pro
3650 3655 3660

Thr Thr His Gln Pro His Gln Thr Trp Leu Ile Ala Ile Pro Glu Thr
3665 3670 3675 3680

Gln Thr His His Pro His Ile Thr Asn Ile Leu Thr Asn Leu His His
3685 3690 3695

His Gly Ile Thr Pro Ile Pro Leu Thr Val Asn His Thr His Thr Asn
3700 3705 3710

Pro Gln His Leu His His Thr Leu His His Thr Arg Gln Gln Ala Gln
3715 3720 3725

Asn His Thr Thr Gly Pro Ile Thr Gly Leu Leu Ser Leu Leu Ala Leu
3730 3735 3740

Asp Glu Thr Pro His Pro His His Pro His Thr Pro Thr Gly Thr Leu
3745 3750 3755 3760

Leu Asn Leu Thr Leu Pro Gln Thr His Thr Gln Thr His Pro Pro Thr
3765 3770 3775

Pro Leu Trp Tyr Ala Thr Thr Asn Ala Thr Thr Thr His Pro Asn Asp
3780 3785 3790

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Gln Pro His His Gln Thr Gln Leu Ala Ile Arg Thr Thr Gly Thr His
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Thr Arg Arg Leu Thr Pro Thr Thr Leu Thr Pro Thr His Gln Pro Pro
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Thr Pro Thr Pro His Gly Thr Thr Leu Ile Thr Gly Gly Thr Gly Ala
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Leu Ala Thr His Leu Thr His His Leu Thr Thr His Gln Pro Thr Gln
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His Leu Leu Leu Thr Ser Arg Thr Gly Pro His Thr Pro His Ala Gln
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His Leu Thr Thr Gln Leu Gln Gln Lys Gly Ile His Leu Thr Ile Thr
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Thr Cys Asp Thr Ser Asn Pro Asp Gln Leu Gln Gln Leu Leu Asn Thr
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Ile Pro Pro Gln His Pro Leu Thr Thr Val Ile His Thr Ala Gly Val
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Asn Leu Phe Ala Pro Val Ser Glu Thr Asp Ala Glu Ser Phe Ser Ser
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Val Thr Ala Ala Lys Ala Thr Gly Ala Ala Ile Leu His Glu Leu Leu

EP 4 324 850 A1

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Glu Arg Glu Val Val Asp Gly Trp Arg Tyr Arg Glu Val Trp Arg Pro
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1905 1910 1915 1920

Arg Ser Gly Glu Arg Pro Val Trp Leu Gly Ser Val Lys Ser Asn Ile
1925 1930 1935

Gly His Ala Gln Ala Ala Ala Gly Val Ala Gly Val Ile Lys Met Val
1940 1945 1950

Met Ala Leu Arg Ala Gly Val Leu Pro Arg Thr Leu His Val Asp Glu
1955 1960 1965

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Pro Ser Ser Gln Val Asp Trp Ser Ser Gly Ser Val Arg Val Leu Ala
1970 1975 1980

Asp Glu Val Glu Trp Pro Gly Val Glu Gly Arg Leu Arg Arg Ala Gly
1985 1990 1995 2000

Val Ser Ala Phe Gly Val Ser Gly Thr Asn Ala His Val Ile Leu Glu
2005 2010 2015

Glu Ala Ser Gly Gly Ala Asp Gly Gly Ala Gly Arg Leu Gln Glu Leu
2020 2025 2030

Gly Pro Gly Val Val Ser Gly Ser Gly Val Val Pro Trp Val Val Ser
2035 2040 2045

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Phe Ala Gln Gln Met Ser Asp Cys Ala Gln Ala Leu Glu Pro Tyr Leu
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Ser Leu Ala Ala Leu Trp Arg Ser Tyr Gly Val His Pro Asp Ala Val
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Tyr Ala Phe Glu Arg Glu Arg Phe Trp Leu Asp Val Glu Gly Ala Pro
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Ala Ala Ala Val Leu Gly His Gly Thr Ala Asp Ala Val Val Pro Glu
2545 2550 2555 2560

Arg Ala Phe Arg Asp Leu Gly Phe Asp Ser Leu Thr Ala Val Glu Leu
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Arg Asn Arg Leu Asn Thr Ala Thr Gly Leu Arg Phe Pro Arg Thr Leu
2580 2585 2590

Val Phe Asp His Pro Arg Pro Val Ala Leu Ala Ala His Ile His Glu
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Gln Leu Ser Gly Gly Ser Pro Thr Thr Gly Thr Ala Leu Ala Leu Ala
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Val Gly Met Ala Cys Arg Phe Pro Gly Gly Val Glu Ser Ala Glu Asp
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Val Lys Ser Asn Ile Gly His Ala Gln Ala Ala Ala Gly Val Ala Gly

Potential SEQ. 0924765

09254605.001

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Val Pro Ala Glu Ala His Val Ile Val Glu Gln Ala Pro Val Glu Ala
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Pro His Val Val Asp Ala Thr Gly Pro Ala Asp Leu Thr Glu Pro Gln
3090 3095 3100

Glu Glu Ala Ala Glu Pro Glu Cys Val Ala Asp Ala Val Thr Glu Met
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Ser Ala Glu Pro Glu Cys Val Ala Asp Ala Met Ser Glu Met Ser Ala
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Glu Cys Val Ala Glu Ala Val Ser Asp Lys Ser Ala Glu Pro Glu Cys
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Val Ala Asp Ala Met Ser Asp Lys Pro Ala Leu Leu Pro Ile Pro Trp
3155 3160 3165

Leu Leu Ser Ala Lys Ser Glu Arg Ala Leu Arg Gly Gln Ala Arg Arg
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Leu Arg Gln Phe Ala Ala Arg Ala Ser Asp Ala Arg Pro Ala Asp Val

3185 3190 3195 3200

Ala His Ala Leu Ala Ala Gln Arg Ser Val Phe Asp His Arg Ala Val
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Val Val Ala Glu Asp Arg Asp Gly Phe Leu Gln Ala Leu Asp Ala Leu
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Ala Glu Gly Arg Ser Ala Asp Gly Leu Ile Glu Gly Ser Val Gly Pro
3235 3240 3245

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3265 3270 3275 3280

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Asp Gly His Leu Asp Gln Pro Leu Arg Pro Leu Ile His Ala Ser Ala
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35 40 45

Phe Pro Gly Gly Val Cys Ser Pro Glu Glu Leu Trp Glu Leu Val Ala
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65 70 75 80

Leu Glu Gly Leu Phe Asp Ser Asp Pro Asp Arg Ser Gly Thr Ser Tyr

JP04-098450 A 19920331

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115 120 125

Arg Leu Leu Leu Glu Thr Ser Trp Glu Ala Phe Glu Arg Ala Gly Ile
130 135 140

Asp Pro Leu Ser Met Arg Gly Ser Arg Thr Gly Val Phe Ala Gly Val
145 150 155 160

Met Tyr His Asp Tyr Gly Ser Arg Leu Gly Thr Ile Pro Glu Gly Phe
165 170 175

Glu Gly Tyr Ile Gly Asn Gly Ser Gly Gly Ala Val Ala Ser Gly Arg
180 185 190

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195 200 205

Ala Cys Ser Ser Ser Leu Val Ala Leu His Leu Ala Cys Gln Ser Leu
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Asn Gln Asp Gly Ala Ser Asn Gly Leu Thr Ala Pro Asn Gly Pro Ala
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340 345 350

Asp Pro Ile Glu Ala Gln Ala Leu Leu Ala Thr Tyr Gly Gln Arg Ala
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370 375 380

Ala Gln Ala Ala Ala Gly Val Gly Gly Val Ile Lys Met Val Met Ala
385 390 395 400

Leu Arg Glu Gly Val Leu Pro Arg Thr Leu His Val Asp Glu Pro Ser
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Gln Gly Gly Gln Trp Ala Gly Met Gly Val Arg Leu Leu Ala Ser Ser
610 615 620

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660 665 670

Met Val Ser Leu Ala Ala Leu Trp Arg Ser Tyr Gly Ile Glu Pro Asp
675 680 685

Ala Val Leu Gly His Ser Gln Gly Glu Ile Ala Ala Ala His Val Cys

690 695 700

Gly Ala Leu Ser Leu Lys Asp Ala Ala Lys Thr Val Ala Leu Arg Ser
705 710 715 720

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725 730 735

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740 745 750

Arg Leu Trp Val Ala Ala Val Asn Gly Pro Arg Ser Thr Ala Val Ser
755 760 765

Gly Asp Ala Glu Ala Val Asp Glu Val Leu Ala Tyr Cys Ala Gly Thr
770 775 780

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785 790 795 800

His Val Gln Pro Leu Arg Glu Glu Leu Leu Glu Leu Leu Gly Asp Ile
805 810 815

Ser Pro Gln Pro Ser Gly Val Pro Phe Phe Ser Thr Val Glu Gly Thr
820 825 830

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835 840 845

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850 855 860

Gly His Arg Val Phe Val Glu Val Ser Pro His Pro Thr Leu Val Pro
865 870 875 880

Ala Ile Glu Asp Thr Thr Glu Asp Thr Ala Glu Asp Val Thr Ala Ile
885 890 895

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900 905 910

Leu Ala His Thr His Thr Thr Gly Ile Gly Thr Pro Thr Thr Trp His
915 920 925

His His Tyr Thr His His His Thr His Pro His Asn His His Leu Asp
930 935 940

Leu Pro Thr Tyr Pro Phe Gln Arg Gln His Tyr Trp Leu Asp Ala Pro
945 950 955 960

Thr Gly Ala Gly Asp Val Ala Ala Ala Gly Leu Glu Pro Ala Glu His
965 970 975

Pro Leu Leu Ala Ala Thr Val Gln Leu Ala Asp Thr Asp Gly Cys Leu
980 985 990

Leu Thr Gly Arg Leu Ser Leu Arg Ser His Pro Trp Leu Gly Asp Tyr
995 1000 1005

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Arg His Leu Ala Gly Val Cys Gly Val Arg Asp Leu Leu Leu Val Ser
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Gln Gly Asn Tyr Ala Ala Ala Asn Ala Ala Leu Asp Ala Leu Ala Tyr
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2005 2010 2015

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Ala Gly Ser Arg Leu Val Val Val Thr Arg Gly Ala Val Val Ala Gly
3170 3175 3180

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Ala Thr Asp Gly Gly Ala Leu Leu Ala Gly Arg Leu Ser Leu Arg Ser
        35                  40                  45

cat ccg tgg ctg gct gac tac gag gtc ggc ggc acg gtg ctg ctg tcg   192
His Pro Trp Leu Ala Asp Tyr Glu Val Gly Gly Thr Val Leu Leu Ser
    50                  55                  60

ggc gcc acc ttc ctc gaa ctc gcc ctt cat gcg ggc aca tac gtg ggc   240
Gly Ala Thr Phe Leu Glu Leu Ala Leu His Ala Gly Thr Tyr Val Gly
65                  70                  75                  80

tgc gac cga gtg gat gag ctg acg ctg cat gcg ccg ctg gtg gtt cct   288
Cys Asp Arg Val Asp Glu Leu Thr Leu His Ala Pro Leu Val Val Pro
                85                  90                  95

gtg gat ggg ggt gtg agt gtg cag gtt ggg gtt gcg gct gcg gat ggg   336
Val Asp Gly Gly Val Ser Val Gln Val Gly Val Ala Ala Ala Asp Gly
            100                 105                 110

gag ggg cgg cgt ttg gtg agt gtg tat gcg cgg ggt ggg agt gct tgt   384
Glu Gly Arg Arg Leu Val Ser Val Tyr Ala Arg Gly Gly Ser Ala Cys
        115                 120                 125
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ggt ggg ggt ggt gcg tcg ggt ggg gtg tgg acg tgt cat gcc tcg ggg 432
Gly Gly Gly Gly Ala Ser Gly Gly Val Trp Thr Cys His Ala Ser Gly
130 135 140

gtg ctg 438
Val Leu
145

<210> 8
<211> 146
<212> PRT
<213> Streptomyces avermitilis

<400> 8
Tyr Trp Leu Glu Ser Thr Gln Pro Gly Ala Gly Asn Val Ser Ala Ala
1 5 10 15

Gly Leu Asp Pro Thr Glu His Pro Leu Leu Gly Ala Thr Leu Glu Leu
20 25 30

Ala Thr Asp Gly Gly Ala Leu Leu Ala Gly Arg Leu Ser Leu Arg Ser
35 40 45

His Pro Trp Leu Ala Asp Tyr Glu Val Gly Gly Thr Val Leu Leu Ser
50 55 60

Gly Ala Thr Phe Leu Glu Leu Ala Leu His Ala Gly Thr Tyr Val Gly
65 70 75 80

Cys Asp Arg Val Asp Glu Leu Thr Leu His Ala Pro Leu Val Val Pro
85 90 95

Val Asp Gly Gly Val Ser Val Gln Val Gly Val Ala Ala Ala Asp Gly
100 105 110

Glu Gly Arg Arg Leu Val Ser Val Tyr Ala Arg Gly Gly Ser Ala Cys
115 120 125

Gly Gly Gly Gly Ala Ser Gly Gly Val Trp Thr Cys His Ala Ser Gly
130 135 140

Val Leu
145

<210> 9
<211> 30
<212> DNA
<213> Artificial Sequence

<220>
<223> Designated is a primer based on the sequence between 9098 and 9127 of SEQ ID NO:1.

<400> 9
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<210> 10
<211> 30
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<213> Artificial Sequence

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<223> Designated is an antisense primer based on the sequence between 9193 and 9222 of SEQ ID NO:1.

<400> 10
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<210> 11
<211> 30
<212> DNA
<213> Artificial Sequence

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<220>
<223> Designated is an antisense primer based on the sequence between 9098 and 9127 of SEQ ID NO:1.

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ccgtgccgcc gacctcgtag tcagccagcc 30

<210> 12
<211> 30
<212> DNA
<213> Artificial Sequence

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<223> Designated is a primer based on the sequence between 8948 and 8977 of SEQ ID NO:1.

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actggctcga aagcacacag cccggtgccg 30

<210> 13
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<212> PRT
<213> Streptomyces avermitilis

<220>
<223> Xaa denotes an unspecified amino acid.

<400> 13
His Xaa Xaa Xaa Gly Xaa Xaa Xaa Xaa Pro
1 5 10

<210> 14
<211> 10
<212> PRT
<213> Streptomyces avermitilis

<220>
<223> Xaa denotes an unspecified amino acid.

<400> 14
His Xaa Xaa Xaa Gly Xaa Xaa Xaa Xaa Ser
1 5 10

<210> 15
<211> 10
<212> PRT
<213> Streptomyces avermitilis

<220>
<223> Xaa denotes an unspecified amino acid.

<400> 15
Tyr Xaa Xaa Xaa Gly Xaa Xaa Xaa Xaa Ser
1 5 10

<210> 16
<211> 10
<212> PRT
<213> Streptomyces avermitilis

<400> 16
His Ala Val Gly Gly Thr Val Leu Leu Ser
1 5 10